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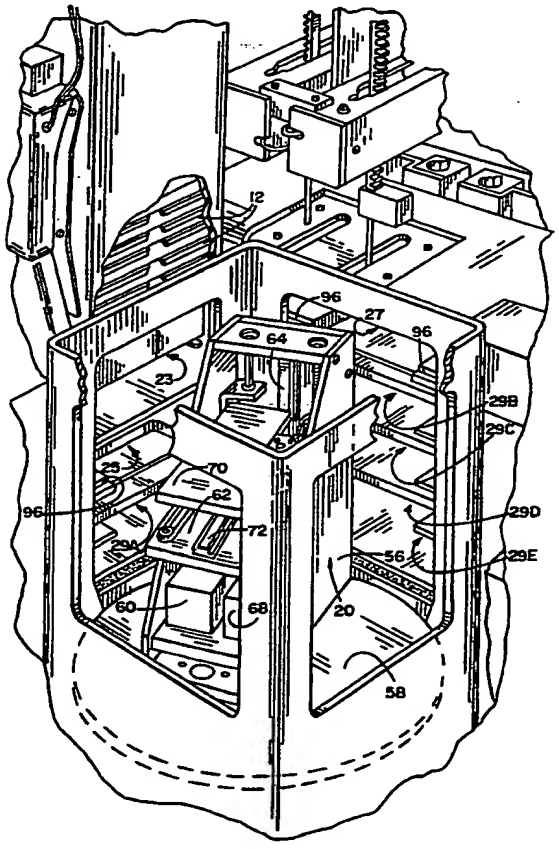
(54) Title: SYSTEMS USING A TEST CARRIER AND ASSOCIATED TRANSPORT MECHANISMS FOR CONDUCTING MULTIPLE ANALYTICAL PROCEDURES

(57) Abstract

Systems for conducting analytical procedures include multiple work stations (22 to 36) that are serviced by a shuttle mechanism (20). The shuttle mechanism (20) conveys materials to and from the work stations (22 to 36) for processing. The systems use a test carrier (12) that is transported by the shuttle mechanism (20) to and from the various work stations (22 to 36). The work stations (22 to 36) themselves include transport mechanisms for moving the test carrier (12) independent of the shuttle mechanism (20). The systems are capable of sequentially transporting a number of test carriers (12) in nonlinear, discontinuous paths among the various processing stations (22 to 36) to thereby perform different prescribed processing tasks upon different carriers (12) at the same time.



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SYSTEMS USING A TEST CARRIER AND ASSOCIATED TRANSPORT MECHANISMS FOR CONDUCTING MULTIPLE ANALYTICAL PROCEDURES

Field of the Invention

The invention relates to analytical systems used in different environments to carry out analytical, laboratory, and clinical procedures. In a more specific sense, the invention also relates to analytical systems that can perform assays in an automated fashion to accurately quantify the presence of targeted compounds within a given sample.

Background of the Invention

A multitude of analytical procedures are in widespread use today in diverse environments to quantify the presence of targeted materials within a given sample. For example, biological analytical procedures can carry out enzyme chemistry assays, DNA probe assays, immunoassays, and cellular or cell surface assays of biological materials using fluorescent, absorbance, and chemiluminescent techniques. Nonbiological analytical procedures can detect the presence of pollutants or toxins in water, air, and soil.

Each given analytical procedure follows its own prescribed protocol, which specifies a carefully timed and prescribed sequence of steps that must be closely followed. Each protocol also specifies other environmental conditions, such as temperature

and humidity, that must be carefully maintained to assure accurate and reproducible results.

Devices that carry out multi-step analytical procedures in an automated or semi-automated fashion are known.

One category of these devices uses a single processing track, along which the various work stations are arranged in linear fashion, one after the other. The processing track conveys the samples to the various work stations. In one variation of this category, parallel processing tracks can be used to increase the throughput of the system.

Another category of multi-step analytical devices uses a rotating carousel arrangement to convey samples to and from one or more various work stations.

Summary of the Invention

The invention provides new systems for conducting multi-step analytical procedures in a highly automated manner that maximizes the throughput of the system, while also assuring accuracy and reproducible results.

According to one aspect of the invention, the system includes a test carrier that retains at least one sample to be analyzed. A discontinuous shuttle member transports the test carrier to and from various processing stations contained within the system. The test carrier retains at least one sample to be analyzed. At least one of the processing stations associated with the system includes its own transport mechanism for moving and positioning the test carrier without reliance upon the shuttle mechanism. The shuttle mechanism is thereby freed to perform other functions while the station performs its slated processing activities.

In one embodiment, the system stores at least one container that retains a component used for processing the samples. In this embodiment, a second transport mechanism operates independently of the first mentioned transport mechanism, and also without reliance upon the shuttle mechanism, for delivering the container to a processing station when the component is needed for a processing task.

In one arrangement, the container stores a quantity of the source specimen that is to be dispensed by a processing station. In another arrangement, the container stores a quantity of a reagent that is to be dispensed by a processing means. In either case, the second transport mechanism conveys the stored component to the processing station for use during the analytical procedure.

In another embodiment, the test carrier retains fluid in first and second spaced apart regions on the carrier. In this way, discrete processing sectors can be defined on the test carrier. The processing station includes at least one pipetting assembly for dispensing aliquots of fluid. The first mentioned transport mechanism moves the test carrier within processing station, without reliance upon the shuttle mechanism, to align a selected one of the regions of the carrier with the pipetting assembly for dispensing the fluid thereto.

In one arrangement, the pipetting assembly receives fluid from a storage container at a first work area within the station and dispenses the fluid to the carrier at a second work area within the station. In this arrangement, a separate third transport mechanism moves the pipetting assembly

between the first and second work areas independently of the first and second transport mechanism and the shuttle mechanism.

In another embodiment, the processing station includes two independently movable pipetting assemblies. In this arrangement, the carrier transport mechanism moves the test carrier within processing station to align a selected one of the regions with a selected one of the pipetting assemblies for dispensing the fluid thereto.

According to another aspect of the invention, a master control mechanism coordinates the operation of the carrier transport mechanism on board the processing station with the operation of the shuttle delivery mechanism outside the processing station. In this aspect of the invention, the carrier transport mechanism operates in a first mode for receiving the test carrier at the processing station access; in a second mode for moving the test carrier for required processing at the processing station; and in a third mode for returning the carrier back to the processing station access. The control mechanism periodically senses the mode of operation of the transport mechanism and generates a signal to operate the shuttle means according to the mode of operation sensed.

In one embodiment, when sensing that the transport mechanism is in its first mode of operation (awaiting the receipt of a test carrier), the control mechanism operates the shuttle mechanism to deliver a carrier to the processing station access. When sensing that the transport mechanism is in its third mode of operation (awaiting the pick up of the test carrier), the control mechanism operates the shuttle mechanism to pick up a carrier

at the processing station access. When sensing that the transport mechanism is in its second mode of operation (busy with the processing of the test carrier), the control mechanism operates the shuttle mechanism in areas outside the work station access.

In one embodiment, the system includes a self-contained compartment for storing a quantity of test carriers. In this embodiment, the carriers are dispensed for pick up by the shuttle mechanism in response to signals generated by the control mechanism upon sensing that the transport mechanism is in its first mode of operation, awaiting the receipt of a carrier.

In a preferred arrangement, the system can sequentially transport several test carriers in nonlinear, discontinuous paths among several processing stations to perform different prescribed processing tasks upon different carriers, all virtually simultaneously and without significant involvement of the user.

Other features and advantages of the invention will become apparent upon considering the accompanying drawings, description, and claims.

Description of the Drawings

Fig. 1 is a front perspective view of the processing module and the master control module associated with the analytical system that embodies the features of the invention;

Fig. 2 is a rear perspective view of the processing module and a portion of the control module shown in Fig. 1, with the lower portion of the processing module housing removed to show parts of the associated power supply, fluid waste system, and environmental control system;

Fig. 3 is an enlarged perspective view of the region of the processing module where the bulk fluid storage containers and associated reservoirs are stored;

Fig. 4 is an enlarged perspective view of the interior of the processing module shown in Fig. 1, looking from the rear of the module, showing the arrangement of associated work stations around the central processing hub;

Fig. 5 is an enlarged perspective view, with portions broken away, of the shuttle member associated with the processing module shown in Fig. 1;

Fig. 6 is an enlarged perspective view of the central hub in which the shuttle member shown in Fig. 5 operates;

Fig. 7 is an enlarged perspective view, with portions broken away and in section, of the central processing hub of the processing module shown in Fig. 1, showing the shuttle member within the processing hub and the arcuate and axially stacked arrangement of some of the associated work stations;

Fig. 8 is a diagrammatic view of the arcuate arrangement of all the work stations about the central processing hub and shuttle member shown in Fig. 7, when viewed from above the processing hub;

Fig. 9 is a perspective view of the top and side portions of the test carrier associated with the analytical system shown in Fig. 1;

Fig. 10 is a top plan view of the test carrier shown in Fig. 9, showing the arrangement of the processing sectors formed thereon;

Fig. 11, is a perspective view of the

interface between the test carrier (shown in Figs. 9 and 10) and the shuttle member (shown in Fig. 5) associated with the analytical system shown in Fig. 1;

Figs. 12 to 15 are a series of perspective views of the shuttle member serving to pick up and drop off the test carrier at a representative work station access within the processing module shown in Fig. 1;

Fig. 16 is a perspective view of a work station having a cover that placed onto and removed from the test carrier as the shuttle member drops off and picks up the test carrier, the cover being shown in its upraised position;

Fig. 17A is an enlarged, exploded perspective view of the mounting assembly for the cover shown in Fig. 16;

Fig. 17B is an enlarged, assembled perspective view of the mounting assembly for the cover shown in Fig. 16, the mounting assembly being shown holding the cover in its upper detent;

Figs. 18 and 19 are a series of perspective views of the shuttle member serving to drop off the test carrier and position the cover at the work station access shown in Fig. 16;

Fig. 20 is an enlarged, assembled perspective view of the mounting assembly for the cover shown in Fig. 16, the mounting assembly being shown holding the cover in its lower detent;

Fig. 21 is a perspective view of the work station shown in Fig 16 with the cover shown in its lowered position upon the test carrier;

Fig. 22 is a diagrammatic view of the interface between the control module and the processing module shown in Fig. 1;

Fig. 23 is a diagrammatic view of the fluid delivery system associated with the processing module shown in Figs. 1 and 2;

Fig. 24 is a diagrammatic view of the waste fluid system associated with the processing module shown in Fig. 1;

Fig. 25 is a diagrammatic view of the environmental control system associated with the processing module shown in Figs. 1 and 2;

Fig. 26 is a front elevation view, in section, of the carrier storage bin associated with the carrier dispensing station of the analytical system shown in Fig. 1;

Fig. 27 is a side elevation view, in section, of the carrier storage bin shown in Fig. 26;

Figs. 28 to 30 are a series of enlarged front elevation views of the hub access region of carrier dispensing station shown in Fig. 26, showing the dispensing of a test carrier from the carrier storage bin into the hub access;

Fig. 31 is a side elevation view, in section, of the hub accesses at the first arcuate position of the shuttle member, showing the transport of the test carrier from the access of the carrier dispensing station to the access of the sample preparation station associated with the analytical system shown in Fig. 1;

Fig. 32 is an enlarged elevation view, with portions in section, of the front region of the processing module shown in Fig. 1, showing the transporter that conveys the test carrier within the sample dispensing station associated with the processing module;

Fig. 33 is an enlarged perspective view,

with portions broken away and in section, of the sample dispensing station associated with the processing module shown in Fig. 1;

Fig. 34 is a region of the sample dispensing station taken generally along line 34-34 in Fig. 33;

Fig. 35 is a front perspective view of a rack for holding source specimens for delivery to the sample dispensing station shown in Fig. 33;

Fig. 36 is a bottom view of the rack taken generally along line 36-36 in Fig. 35;

Fig. 37 is an enlarged side sectional view of a rack transport mechanism associated with the sample dispensing station shown in Fig. 33;

Fig. 38 is an enlarged side sectional view of a rack transport mechanism associated with the sample dispensing station taken generally along line 38-38 in Fig. 33;

Fig. 39 is an enlarged front perspective view, with portions broken away, of the sample dispensing station;

Fig. 40 is an enlarged perspective view of the sample pipetting pumping mechanisms associated with the sample dispensing station shown in Fig. 33;

Fig. 41 is a perspective view of one of the sample pipetting pumping mechanisms taken generally along line 41-41 in Fig. 40;

Fig. 42 is a diagrammatic summary of the sequence of operation of the pipetting pumping mechanisms associated with the sample dispensing station shown in Fig. 26;

Fig. 43 is an enlarged side sectional view of a wash well associated with system shown in Fig. 1;

Fig. 44 is a side section view of the wash

well with a probe inserted in its first wash chamber;

Fig. 45 is a side section view of the wash well with a probe inserted in its second wash chamber;

Fig. 46 is a side section view of the wash well with a probe inserted in its third soak chamber;

Fig. 47 is an enlarged sectional view of a heater and liquid level sensor associated with the sample pipetting pumping mechanism of the sample dispensing station;

Fig. 48 is an enlarged perspective view, with portions broken away and in section, of the reagent dispensing station associated with the processing module shown in Fig. 1, when viewed from the interior of the module;

Fig. 49 is a top plan view, with portions broken away, of the reagent delivery carousel associated with the reagent dispensing station shown in Fig. 48;

Fig. 50 is a perspective view of the reagent vials and associated holder carried by the reagent delivery carousel shown in Fig. 49;

Fig. 51 is an enlarged perspective view of an integrated three-vial reagent pack transported by the reagent delivery carousel;

Fig. 52 is a top view of the three-vial reagent pack carried within the reagent delivery carousel;

Fig. 53 is an enlarged perspective view of a user placing a three-vial reagent pack into the reagent delivery carousel;

Fig. 54 is an enlarged perspective view of the combined washing and substrate dispensing

stations associated with the processing module shown in Fig. 1;

Fig. 55 is an enlarged perspective, with portions broken away, of the region of the washing station shown in Fig. 54 where the washing pipette assembly is located;

Fig. 56 is an enlarged elevation view of the transporter associated with the combined washing and substrate dispensing system shown in Fig. 44;

Figs. 57 to 59 are a series of drawings showing the operation of the washing pipette assembly shown in Fig. 55;

Fig. 60 is an enlarged elevation view, with portions broken away and in section, of the reader station associated with the processing module shown in Fig. 1;

Fig. 61 is an enlarged perspective view, with portions broken away of the optical assembly associated with the reader station shown in Fig. 60;

Fig. 62 is an enlarged perspective view, with portions broken away, of the transporter associated with the reader station shown in Fig. 60;

Fig. 63 is an enlarged perspective view of the carrier disposal station associated with the processing module shown in Fig. 1;

Figs. 64 and 65 show the sequence of operation of the carrier disposal station shown in Fig. 63, taken generally along line 64-64 in Fig. 63; and

Fig. 66 and 67 are diagrammatic time lines showing the sequence of certain protocols conducted by the analytical system shown in Fig. 1.

Description of the Preferred Embodiments

I. OVERVIEW OF THE SYSTEM AND ITS COMPONENTS

The drawings show a system 10 for conducting analytical procedures that incorporates the features of the invention. The analytical system 10 is applicable for use in different environments to carry out diverse types of analytical, laboratory, and clinical procedures.

For example, the invention has broad application in performing all types of assays in an automated fashion to accurately quantify the presence of targeted compounds within a given sample. In this environment, the invention can be used to carry out enzyme chemistry assays, DNA probe assays, immunoassays, and cellular or cell surface assays of biological materials using fluorescent, absorbance, and chemiluminescent techniques.

The invention also has application in detecting the presence of the testing of nonbiological materials, such as pollutants in water, air, and soil. Certain aspects of the invention also have broad application in laboratory pipetting systems in general, and in comparable clinical, medical, and industrial environments that require accurate and reproducible transfers of fluid samples.

In this Specification, the system 10 will be described in the specific functional context of a blood assay device for screening human blood serum/plasma.

Blood assay analyses follow various prescribed protocols that differ depending upon the biological substances in the sample that are to be detected and quantified. Each protocol specifies a carefully timed and prescribed sequence of steps that must be closely followed. Each protocol also specifies other environmental conditions, such as temperature

and humidity, that must be carefully maintained to assure accurate and reproducible results.

In this environment, the analytical system 10 includes three major components parts: a test carrier 12 (best shown in Figs. 9 and 10), a processing module 14, and a master control module 16 (best shown in Figs. 1 and 2). The component parts will first be described in a general fashion to define their individual function and to identify the principal relationships among them. A more detailed description of these component parts will then follow in the specific context of the procedures performed in the illustrated and preferred embodiments.

A. The Test Carrier

The test carrier 12 serves to contain one or more samples of fluid for analysis by the system 10. The carrier 12 holds the samples throughout the processing procedure.

As Figs. 9 and 10 show, the test carrier 12 includes a series of test wells 18 aligned in a predefined relationship. Each test well 18 retains a prescribed aliquot (or sample) of the biological fluid to be analyzed.

The form and construction of the test carrier 12 can of course vary according to the assay procedures and techniques selected. For example, the carrier 12 can take the form of a rack that retains one or more individual test tubes, each of which constitutes a "test well" as this Specification uses that term.

In the illustrated and preferred embodiment shown in Figs. 9 and 10, the test carrier 12 takes the form of a tray of unitary molded construction

made of an inert plastic or another lightweight inert material, such as glass. In the illustrated embodiment, the carrier 12 is molded from a polystyrene-based plastic polymer and is intended to be a single use, disposable component of relatively low cost.

As Figs. 9 and 10 show, the molded test wells 18 form a prescribed matrix consisting of twelve linear columns C1 to C12 (extending vertically in Fig. 10) and eight linear rows R1 to R8 (extending horizontally in Fig. 10).

The prescribed arrangement of test wells 18 in the matrix makes it possible to establish discrete processing sectors upon the carrier 12. Each processing sector can contain one or more samples and can be dedicated to the performance of one selected blood assay procedure on all the contained samples. The samples can originate from either the same or a different fluid source.

In the illustrated embodiment, each complete column on the carrier 12 defines a "processing sector" as this Specification uses that term. Each processing sector contains eight test wells 18, which corresponds to the number of rows in each column. For ease of description, the processing sectors will be described by their column number on the tray (C1 to C12), and the test wells 18 will be described by their row number within their respective columns (R1 to R8). For example, the third test well 18 in the fourth processing sector will be identified as well C4, R3 (or, alternatively, well R3, C4).

In the illustrated embodiment, the analytical system 10 performs six separate blood assays on human blood serum/plasma for the following analytes:

(1) Hepatitis type B surface antigen (HBs Ag);
(2) Hepatitis type B core antibody (HBc Ag);
(3) Human immuno deficient virus antibody (HIV-1);
(4) Human T-cell lymphotrophic virus (type 1) antibody (HTLV-I);
(5) T. Pallidum (syphillis) antibody (TPA Ab); and
(6) Glutamate pyruvate transaminase (GPT or ALT).

Of the above, assays (1) to (5) are immunoassays, while assay (6) is an enzyme chemistry.

To accommodate these different blood assay procedures, the processing matrix established on the carrier 12 creates two pairs of six processing sectors (for a total of twelve processing sectors), as follows (also refer to Fig. 10):

Processing Sectors C1 and C7 : HBs Ag;
Processing Sectors C2 and C8: HBc Ag;
Processing Sectors C3 and C9: ALT;
Processing Sectors C4 and C10: HIV-1;
Processing Sectors C5 and C11: HTLV-I; and
Processing Sectors C6 and C12: TPA Ab.

Up to eight samples can be contained within each processing sector, one for each row R1 to R8.

Therefore, in the illustrated embodiment, the carrier 12 can accommodate as many as six different blood assay procedures on as many as sixteen different source samples. A single test carrier 12 thus can perform a total of ninety-six blood assay procedures.

B. <u>The Processing Module</u>

The processing module 14 is a self-

contained unit that performs all the various steps of the selected analytical procedure or procedures automatically from beginning to end, without significant operator intervention.

Please refer now principally to Figs. 1 to 8. As these drawings show, the processing module 14 includes within a common housing several processing stations 22 to 36 that are individually serviced by a shuttle member 20. The shuttle member 20 transports the test carrier 12 to the various processing stations 22 to 36. The processing stations 22 to 36 in turn perform one or more prescribed processing tasks on the samples contained in the test carrier 12. As will be described in greater detail later, using the shuttle member 20, the processing module 14 can sequentially transport several test carriers 12 in discontinuous paths among the various processing stations 22 to 36, in this way simultaneously performing different prescribed processing tasks upon different carriers 12.

1. <u>The Processing Stations</u>

Each processing station 22 to 36 performs one or more prescribed processing tasks upon the samples contained within the various processing sectors on the carrier 12.

In the illustrated and preferred embodiment, most of the processing stations 22 to 36 are multi-functional and can distinguish between the various processing sectors defined on the carrier 12 in terms of tasks to be performed. The multi-functional stations thereby perform one prescribed processing task (or step) within one processing sector of the carrier 12 and perform a

different prescribed processing task (or step) within another processing sector of the carrier 12. In this way, the processing module 14 can perform immunoassay procedures according to many different protocols on the different source samples contained on a single test carrier 12.

In the illustrated and preferred embodiment, many processing stations 22 to 36 can move and position the carrier 12 independent of the shuttle member 20. This will be described in greater detail later.

The number of the processing stations can of course vary according to the number and type of processing tasks that are to be performed by the analytical system 10. The blood assay procedures of the kind performed in the illustrated embodiment generally involve the addition of one or more specified reagents, buffers, and/or diluents (which will be collectively called "reagents") to a specified volume or sample of the fluid obtained to be analyzed. The sample/reagent mixture is incubated one or more times to form a solid phase bound complex that typically includes an enzyme label. After incubation, the sample/reagent mixture is usually washed one or more times to remove the "free" or otherwise nonspecifically bound components, and a substrate is added. The enzyme label on the complex serves as a catalyst that splits the substrate, in the process forming a molecule that can be detected and quantitatively measured. In the illustrated embodiment, the formed molecule fluoresces, and it is this fluorescence that is detected. Alternatively, an enzyme label that itself fluoresces without a substrate can be used.

All the blood assays performed in the illustrated embodiment, except ALT, employ a so-called "solid phase" assay technique. This technique relies upon a solid support of immunosorbent material to bind the complexes. Solid supports like small paramagnetic particles, filter paper, plastic balls, polysaccharide beads, or the interior walls of test tubes can be used for this purpose. In the illustrated embodiment, the analytical system 10 will be described using procedures employing mobile paramagnetic particles as solid phase binding sites. Preferred analytical procedures employing paramagnetic particles and fluorescent substrates are described in U.S. Patent Application No. entitled

In the illustrated embodiment, the processing stations are established to do eight generic processing tasks that are, for the most part, common to all the six immunoassays performed. In this arrangement, the processing module 14 includes the following principal processing stations (see Figs. 1, 3, and 6):

(1) Processing station 22 is a carrier dispensing station for storing and dispensing the one or more test carriers 12;

(2) Processing station 24 is a sample dispensing station for receiving multiple sources of biological fluids and for dispensing samples of biological fluids from these sources into the wells 18 of the test carrier 12;

(3) Processing station 26 is a reagent dispensing station for dispensing one or more reagents into the samples contained in wells 18 of the test carrier 12;

(4) Processing station 28 is at least one incubation

station for incubating the sample and reagent mixtures (in the illustrated embodiment, there are nine incubation stations, designated 28 A to I);

(5) Processing station 30 is a washing station for removing unbound materials from the samples;

(6) Processing station 32 is a substrate dispensing station for adding substrate from which the fluorescent molecule is formed for detection;

(7) Processing station 34 is a reader station for determining the presence and concentration of the fluorescent molecule; and

(8) Processing station 36 is a carrier disposal station for disposing of the test carrier 12 once all the processing steps are completed.

As Fig. 22 shows, each processing station 22 to 36 includes its own dedicated control mechanism that directs the associated station to perform one or more specified tasks in response to commands from the control module 16 (this will be described in greater detail later). The processing module 14 includes a self-contained DC power supply 38 of conventional construction (also see Fig. 2) for these control mechanisms and the associated components.

Each processing station 22 to 36 comprises a self-contained module than can operate as a "stand alone" system, out of association with other processing stations shown. When in association with other stations (as in the illustrated embodiment), the modular nature of each processing station 22 to 36 simplifies removal, repair, and replacement of each station to simplify routine maintenance, troubleshooting, and repair.

The processing module 14 also includes

various self-contained systems that support the operation of the processing stations, as follows:

(1) A self-contained fluid delivery system 40 (which Fig. 23 shows in detail) conveys fluid to the various processing stations from six bulk fluid containers 42 (designated in Fig. 23 as B1 to B6) via six holding reservoirs 43 (designated in Fig. 23 as R1 to R6). The containers 42 and reservoirs 43 are all stored within an accessible front compartment 44 in the module 14 (see Figs. 1 and 3). When emptied of solution, the containers 42 are removed and replaced with fresh containers 42. The reservoirs 43 are permanently installed within the processing module 14.

The bulk containers B1 and B2 hold the solution and buffer used by the sample preparation station 24. The bulk container B3 holds the solution used by the reagent dispensing station 26. The bulk container B4 holds the solution used by the washing station 28. The bulk container B5 holds the substrate used by the substrate dispensing station 32. The bulk container B6 holds the pipette soaking solution used by the sample dispensing, reagent dispensing, washing, and substrate dispensing stations.

Individual pumps (designated P1 to P6 in Fig. 23) deliver fluids from a container 42 to its associated reservoir 43. As Fig. 3 shows, each reservoir 43 includes a high fluid level sensor 112 and a low fluid level sensor 114, which toggle the associated pump on and off. When the fluid level within a given reservoir 43 drops below the high level sensor 112, a signal

is generated to turn the associated pump on to deliver fluid to the reservoir 43. When the fluid level within a given reservoir 43 rises above the high level sensor 112, a signal is generated to turn the associated pump off When the fluid drops below the low level sensor 114, all processing stops.

The master control module 16 establishes a maximum time period for running the associated pump after the high level sensor 112 toggles the pump on to replenish the reservoir 43. If the high level sensor 112 does not detect the presence of fluid within this time period, the master control module 16 disables the associated pump and generates an alarm signal for the user.

Usually, this "time out" condition will occur when the associated bulk fluid container 42 empties. Since the control module 16 disables only the associated pump, the user is able to remove and replace the empty container with a new, filled bulk fluid container 42 without otherwise interrupting system operation. The user is therefore able to change bulk fluids "on the fly," without shutting down the entire system 10.

(2) A self-contained fluid waste system 46 (which Fig. 24 shows in detail) conveys waste fluids generated during the procedures to a waste fluid container 48 stored within another compartment 50 in the module 14 (see Fig. 1).

The waste fluid circuit 46 includes a vacuum pump 316 that draws waste fluid from the system 10 into a waste fluid reservoir 318. An inline hydrophobic filter 320 prevents contaminants, such as bacteria and pathogens,

carried by the waste fluid from entering the vacuum pump 316 and being dispelled into the atmosphere.

An intermittently operated discharge pump 322 draws fluid from the waste fluid reservoir 318 into the waste fluid container 48, that itself contains a suitable disinfectant for destroying any bacteria or pathogenic materials carried in the waste fluid. A fluid level sensor 324 in the reservoir 318 toggles the discharge pump 322 on and off.

As Fig. 1 shows, an optical sensor 47 detects the presence of the waste fluid container 48. Another sensor 49 detects the opening of the door 53 to the compartment 50. As Fig. 23 shows, when the sensor 49 detects the door 53 is open, or the sensor 47 detects that the waste fluid container 48 is not present, the control module 16 disables the waste pump 322. Only when the container 48 is present and the door 53 is closed will the control module 16 allow the waste pump 322 to operate. The user is therefore able to empty or replace the waste fluid container 48 "on the fly," without shutting down the entire system 10.

A strain gauge 55 senses the weight of the waste fluid container 48. When the weight reaches a prescribed amount, a signal is generated to tell the operator to empty the container 48. If the operator does not respond within a prescribed time period, the control module 16 disables the waste pump 322 until the operator empties the container 48 in the manner described above.

(3) A self-contained environmental control system 52

(which Fig. 25 shows in detail) monitors and maintains prescribed temperature and humidity conditions within each processing station 22 to 36. As will be described later, some elements of the environmental control system 52 are enclosed within a compartment 51 in the module 14 (see Fig. 2), while other elements are part of the various work stations. In the illustrated embodiment, temperatures in the range of between 30 and 45 degrees centigrade (and preferably about 42 degrees centigrade) are maintained by the system 52.

Other aspects of these self-contained support systems 40, 46, and 52 will be described in greater detail later.

a. **The Shuttle Member**

The shuttle member 20 (see Figs. 5 to 7) transports individual test carriers 12 to and from each processing station 22 to 36. The shuttle member 20 also includes its own dedicated control mechanism (as Fig. 22 shows), connected to the DC power supply 38. The control mechanism operates the shuttle member 20 according to prescribed command signals received from the control module 16. The shuttle member 20 therefore constitutes yet another modular component of the processing module 14.

The shuttle member 20 is movable in three distinct directions:

(1) In one direction (shown by arrows designated A in Fig. 5), the shuttle member 20 rotates about an axis 54 in a 360-degree arc, or in prescribed smaller increments thereof.

(2) In another direction (shown by arrows designated B in Fig. 5), the shuttle member 20 moves one up

and down in a prescribed range of positions located axially along the rotational axis 54.

(3) In a third direction (shown by arrows designated C in Fig. 5), the shuttle member 20 moves in a prescribed range of positions radially toward and away from the rotational axis 54.

The shuttle member 20 and its associated platform can be variously constructed. In the illustrated embodiment (best shown overall in Fig. 5), the shuttle member 20 includes a support frame 56 attached to a turntable 58. A first stepper motor 60 rotates the turntable 58 about the axis 54, along with the attached frame 56. The first stepper motor 60 operates in response to signals received from the shuttle control mechanism.

The support frame 56 carries a movable deck 62. The deck 62 is movable on the frame 56 in a trackway 64 that extends generally parallel to the rotational axis 54 of the turntable 58. A drive screw 66 coupled to a second stepper motor 68 advances the deck 62 up and down along the trackway 64. The second stepper motor 68 also operates in response to signals received from the shuttle control mechanism.

In the illustrated arrangement, clockwise rotation of the drive screw 66 advances the deck 62 downward along the rotational axis 54 (toward the turntable 58). Counterclockwise rotation of the drive screw 66 advances the deck 62 upward along the rotational axis 54 (away from the turntable 58).

A shuttle platform 70 is itself movable upon the deck in another trackway 72 that extends radially of the rotational axis 54 of the turntable 58. A belt drive 74 coupled to a third stepper motor 76 advances the platform 70 along this

trackway 72 toward and away from the rotational axis 54. The third stepper motor 76 also operates in response to signals received from the shuttle control mechanism.

In the illustrated arrangement, the shuttle platform 70 moves in its first direction (Arrows A) as the turntable 58 rotates (by actuating the first stepper motor 60); in its second direction (Arrows B) as the deck 62 moves up and down (by actuating the second stepper motor 68); and in its third direction (Arrows C) as the platform 70 moves in and out upon the deck 62 (by actuating the third stepper motor 76).

b. Transport of the Test Carrier by the Shuttle Member

Please refer now principally to Figs. 9 to 15. As these drawings show, the shuttle platform 70 is movable into and out of secure engagement with the test carrier 12 for transporting the carrier 12 among the various processing stations 22 to 36. The test carrier 12, the shuttle platform 70, and the processing stations 22 to 36 are each specially configured for this purpose.

More particularly, the test wells 18 of the carrier 12 generally terminate along a common base plane 84 (see Fig. 9). The test carrier 12 also includes two pairs of opposing sidewalls 78(A and B) and 80 (A and B). The first pair of sidewalls 78A/B extends parallel to the prescribed rows of the test wells 18. The second pair of sidewalls 80A/B extends parallel to the prescribed columns of test wells 18. As Fig. 9 shows, the first sidewalls 78A/B commonly terminate below the base plane 84 of the wells 18. The second sidewalls 80A/B terminate

above the base plane 84 of the wells 18.

A notched keyway 82 (A and B) is formed in each first sidewall 78A/B, with the uppermost edge 84 of each keyway 82A/B extending above the base plane 84 of the wells 18. The two keyways 82A/B are generally axially aligned with each other on their respective sidewalls 78A/B. The first sidewalls 78A/B also each terminates with a flanged bottom edge 86A/B that extends from opposite sides of the keyway 82A/B along the entire width of the carrier 12.

The shuttle platform 70 (see Fig. 11) includes a transverse groove 88 and an upwardly raised keyway 90 within the groove 88. The groove 88 and raised keyway 90 on the shuttle platform 70 mutually capture one flanged bottom edge and associated keyway (either 86A and 82A or 86B and 82B) on the carrier 12, depending upon the orientation of the carrier 12. This cooperation of interlocking parts secures the carrier 12 on the platform 70 for transport (as Fig. 12 shows).

As Figs. 6 to 8 best show, the processing module 14 includes several shuttle accesses (which are generally identified by reference numerals 23, 25, 27, 29, 31, and 35) associated with the processing stations 22 to 36, where the carrier 12 can be picked up and dropped off by the shuttle platform 70.

Figs. 12 to 15 show a representative shuttle access. The access has a support surface 92 and cutout portion 94. The cutout portion 94 is wider than the shuttle platform 70 and associated deck 62, but not as wide as the carrier 12 measured along the first sidewalls 78A/B.

When properly supported on the surface 92

(see Fig. 13), the carrier 12 spans the cutout portion 94 with the notched carrier keyways 82A/B positioned generally along the centerline of the cutout portion 94.

As Figs. 12 to 15 show, these mutually complementary configurations enable the transport by the shuttle member 20 of the carrier 12 to and from the various processing stations 22 to 36.

To bring the shuttle platform 70 into engagement with a test carrier 12 supported in a given access support surface 92 (see Figs. 14 and 15), the third stepper motor 76 moves the shuttle platform 70 in its radial direction (Arrow C) into a prescribed pick up position. In this position (shown in Fig. 15), the shuttle platform 70 is located centrally below the cutout portion 94 on which the carrier 12 rests, with the flanged bottom edge 86B and keyway 82B of the rearwardmost carrier sidewall 78B registering in alignment with the groove 88 and keyway 90 of the platform 70.

The second stepper motor 68 then raises the shuttle platform 70 in its axial path (Arrow B) into contact with the bottom of the wells 18, i.e., the base plane 84 of the carrier wells 18 shown in Fig. 9. This movement lifts the carrier 12 off the access surface 92 (as Fig. 12 shows).

As the platform 70 raises to lift the carrier 12, the platform groove 88 captures and engages the flanged bottom edge 86B of the rearwardmost carrier sidewall 78B. The platform keyway 90 simultaneously captures the associated notched keyway 82B formed in that carrier sidewall 78B.

The upwardly raised second sidewalls 80A/B allow the platform 70 to make supporting contact

uniformly across the entire base plane 84 of the wells 18, in this way maximizing the area of supporting contact between the platform 70 and the carrier 12.

As Fig. 12 shows, the lateral and transverse dimensions of the carrier 12 exceed the corresponding dimensions of the shuttle platform 70 and underlying deck 62. Thus, when the engagement between the mating components occurs, a portion of the carrier 12 overhangs each side and leading edge of the shuttle platform 70 and underlying deck 62.

When these engagements between the mating components occur, the carrier 12 is effectively locked into a secure transport position upon the shuttle platform 70 (see Fig. 12). The mating connections between the platform 70 and the carrier 12 prevent sliding movement of the carrier 12 upon the platform 70 as the platform 70 moves in its various paths to transport the carrier 12.

The carrier 12 is removed from the shuttle platform 70 and deposited upon the desired access support surface 92 by following a generally reverse sequence of steps, shown in Figs. 12 and 13. The first stepper motor 60 aligns the shuttle platform 70 with the selected carrier support surface 92. The third stepper motor 76 moves the platform 70 (Arrow C) into a drop-off position above the cutout portion 94 (as Fig. 12 shows). The second stepper motor 68 lowers the platform 70 (Arrow B), bringing the carrier 12 to rest on the support surface 92 and raising the flanged bottom carrier edge 86B out of the platform groove 88, simultaneously separating the two keyways 82B from 90 (see Fig. 13).

As Figs. 12 to 15 show, the access support surface 92 preferably also includes one or more

transverse grooves 96 to capture the flanged edges 86A/B of the carrier 12 and hold the carrier 12 in position. The access support surface may also include a keyway 97 to mate with the key 82A/B on the carrier.

The access support surface 92 can also include a mechanism for moving the carrier 12 on the support surface 92 independent of the shuttle member 20. This will be described in greater detail later.

As Figs. 16 to 21 show, certain work stations include covers 93 for the carrier 12 held on the access support surface 92. The covers 93 control the temperature and prevent evaporative fluid loss from the wells 18 during processing. In the illustrated and preferred embodiment, all incubation stations 28 A to I include a cover 93.

The shuttle member 20 places the cover 93 on the carrier 12 while depositing the carrier 12 at an incubation station 28. The shuttle member 20 removes the cover 93 from the carrier 12 while transporting the carrier 12 from an incubation station 28, leaving the cover 93 behind at the work station.

More particularly, each cover includes an inner lip 103 and an outer lip 105. The outer lip 105 of each cover 93 is suspended on a pair of pins 95. Each pin 95 is engaged in a track 97 having an upper detent 99 and a lower detent 101.

When the pins 95 mutually rest in the upper detent 99 (as Figs. 16 and 17A/B show), the outer lip 105 of the cover 93 is suspended above the support surface 92. This allows the shuttle platform 70 to radially transport the carrier 12 into the associated access beneath the cover 93 (as Arrow C shows in Fig. 18). The forward carrier edge

78A engages the inner lip 103 of the cover 93.

Slight upward axial movement (Arrow B) as the shuttle platform 70 moves radially into the access frees the pins 95 from their upper detents 99 (as Fig. 18 shows). At the same time, the rear carrier edge 78B engages the outer lip 105 of the cover 93.

As the shuttle platform 70 next moves axially downward (Arrow B in Fig. 19), the carrier 12 comes to rest on the support surface 92. The pins 95 slide within the tracks 97 into the lower detent 101. The shuttle platform 70 radially withdraws (Arrow C in Fig. 19), leaving the now covered carrier 12 behind on the support surface 92, as Figs. 20 and 21 show.

Removal of the cover 93 as the shuttle platform 70 transports the carrier 12 out of the access follows the reverse sequence of steps. Axial upward movement of the shuttle platform 70 lifts the carrier 12 from the support surface 92, freeing the pins 95 from their lower detents 101. Radial movement of the platform 70 out of the access combined with downward axial movement brings the pins 95 to rest within their upper detents 99, lifting the outer cover lip 105 from the carrier 12. Continued radial movement transports the carrier 12, without the cover 93, from the access.

As Figs. 11 to 15 show, the shuttle member 20 preferably includes a position sensor 98 for detecting the presence of the test carrier 12 upon the shuttle platform 70. In the illustrated embodiment, the position sensor 98 comprises an emitter that transmits an infrared beam toward the underside of the test carrier 12. The position sensor also comprises a detector that receives the

infrared beam after being reflection off the underside of the test carrier 12, if the test carrier 12 is properly positioned upon the shuttle platform 70.

The shuttle control mechanism actuates the position sensor 98 to assure that the shuttle platform 70 properly engages the test carrier 12 after the pick up operation. The shuttle control mechanism also actuates the position sensor 98 to assure that the test carrier 12 has been removed from the shuttle platform 70 after the drop-off operation. The shuttle control mechanism also periodically actuates the position sensor 98 while the shuttle platform 70 is in transit between its prescribed pick up and drop-off points to assure that the test carrier 12 has not been dislodged.

The lack of a reflective signal when the test carrier 12 should be present upon the shuttle platform 70, or the presence of a reflective signal when the test carrier 12 should not be present, transmits an error signal to the control module 16. Upon receipt of the error signal, the control module 16 provides an error message to the operator and suspends operation of the system 10 until the error is corrected.

2. The Central Hub

Please refer now principally to Figs. 6 to 8. As these drawings show, the different processing stations 22 to 36 are positioned around the multi-directional shuttle member 20 in an arcuately spaced and vertically stacked relationship. In this configuration, the shuttle member 20 operates from within an enclosed, stationary center hub 100 to obtain access to all the processing stations. The

hub 100 is axially aligned with the rotational axis 54 of the shuttle member 20. Access can be obtained by moving the shuttle member 20 in a variety of discontinuous rotational, axial, and radial paths about its rotational axis 54.

The specific arrangement of the processing stations for access through the center hub 100 can of course vary. In the illustrated embodiment (see Figs. 7 and 8), the station arrangement provides access through the center hub 100 generally at four arcuately spaced locations, designated A1 to A4 in Fig. 8.

Accesses 23/25/29A to the carrier dispensing station 22, the sample dispensing station 24, and one incubation station 28A (respectively) are provided through the center hub 100 at the first arcuate location A1. At this location, the hub access 23 for the carrier dispensing station 22 is stacked vertically above the hub access 25 for the sample dispensing station 24, as measured along the rotational axis 54 of the shuttle member 20. The hub access 29A for the incubation station 28A is also stacked vertically below the hub access 25 for the sample dispensing station 24. In the illustrated arrangement, the vertically stacked accesses 23, 25, and 29A are generally axially aligned along the rotational axis 54 of the shuttle member 20, that is, they are directly one atop the other.

Accesses 27/29B-E to the reagent dispensing station 26 and four additional incubation stations 28 B/C/D/E (respectively) are provided through the center hub 100 at the second arcuate location A2. At this location, the hub access 27 to the reagent dispensing station 26 is stacked vertically above

the hub accesses to the additional incubation stations 29 B/C/D/E, as measured along the rotational axis 54 of the shuttle member 20. The accesses 29 B/C/D/E are themselves also further vertically stacked one above the other. The vertically stacked accesses 27 and 29 B/C/D/E are all axially aligned along the rotational axis 54 of the shuttle member 20, one atop the other.

Access 31 to the washing station 30 and the substrate dispensing station 32 is provided through the center hub 100 at the third arcuate location A3. At this location, both stations 30 and 32 share a common hub access 31. Accesses 29 F/G/H/I to four additional incubation stations 28 F/G/H/I are also provided at the third arcuate location A3, vertically stacked one above the other beneath the common hub access 31 for the washer and substrate dispensing stations 30 and 32. The vertically stacked accesses 31 and 29 F/G/H/I are all axially aligned along the rotational axis 54 of the shuttle member 20.

Access 35 to the reader station 34 and the carrier disposal station 36 is provided through the center hub 100 at the fourth arcuate location A4. At this location, the reader station 34 is positioned above the disposal station 36. However, the reader and the disposal stations 34 and 36 share a common, somewhat vertically enlarged access 35.

It should be appreciated that additional processing stations can be added to the central hub 100 by arrangement at additional arcuate locations and by stacking in other vertical directions up and down along the central hub 100. Also, it should be appreciated that, due to the multi-directional movement of the shuttle member 20, the vertically

stacked accesses need not be mutually aligned one above the other about the rotational axis 54 of the shuttle member 20.

The arrangement of the central hub 100 to access all the processing stations 22 to 36 creates a compact operating zone that allows the processing stations 22 to 36 to be vertically stacked one atop the other, as the illustrated and preferred embodiment shows. The processing module 14 is thereby provided with a relatively small "footprint," despite the presence of many work stations.

3. Control of Environment Within the Central Hub 100

The compact size of the central operating hub 100 also simplifies the control of humidity and temperature within the processing regions of the module 14.

More particularly, the environmental control system 52 (see Figs. 2 and 25) includes a central humidity control subsystem 102 that services the operating hub 100. The subsystem 102 is located in a rear compartment 51 of the module 14 (as Fig. 2 shows). The subsystem 102 includes a humidifier 104 that draws air at ambient room temperature and conveys treated air at a final desired temperature of between thirty and forty-five degrees centigrade and a relative humidity level of about 70% into the hub 100 through an outlet opening 116 located adjacent the access 35. The heated and humidified air fills the entire central hub 100 access area and disperses into the interconnected regions of the processing stations 22 to 36.

In addition (and as will be described

later), the environmental control system 52 also further monitors and controls the temperatures within the work stations 22 and 36. The work stations are enclosed with foam insulation 106 (see Fig. 4) to maintain proper internal temperatures.

c. The Master Control Module

The master control module 16 (best shown in overall view in Fig. 1) issues the appropriate command signals to the various control mechanisms of the processing stations 22 to 36 to sequence the overall operation of the processing module 14 according to the protocol established for each analytical procedure selected to be performed. Cables 118 link the master control module 16 to the processing module 14 (as Fig. 2 shows).

The master control module 16 includes a housing 120 that encloses a main microprocessor based CPU 122 (see Fig. 22 also). The CPU 122 issues the prescribed command signals to the various control mechanisms for the shuttle member 20 and processing stations 22 to 36 carried within the processing module 14. The CPU 122 also issues periodic status inquiries to the various control mechanisms to assure that the control mechanisms are operating according to the planned sequence and no failures have occurred.

In general operation, upon receiving a status inquiry, a given control mechanism will send back a "Busy" signal if it is then engaged in a task and a "Not Busy" signal if the task has been completed and a further command signal is desired. In this master-slave relationship, the CPU 122 coordinates and controls the overall operation of the processing module 14.

While various arrangements are possible, in the illustrated embodiment (see Fig. 18), the CPU 122 comprises an IBM PC compatible CPU board that allows multi-tasking sequences. Various input/output (I/O) devices communicate with the main CPU 122 through conventional data and address busses 124 and 126. Various arrangements are possible. In the illustrated embodiment, the input device takes the form of a conventional keyboard 128, and the output devices take the form of a conventional video monitor 130 and printer 132 (as Fig. 1 also shows).

A mass storage device 134 for storing digital information also communicates with the main CPU 122 through the busses 124 and 126. The mass storage device 134 retains a master control schedule 590 in its internal memory. The master control schedule 590 consolidates the various process requirements of the individual protocols, such as step sequence, step timing, and other operating parameters.

The command signals issued by the CPU 122 to the individual control mechanisms of the shuttle member 20 and the processing stations 22 to 36 are derived based upon the master control schedule 590. The master control schedule 590 coordinates the transport of the test carriers 12 to and from the various processing stations 22 to 36 in concert with the operation of the processing stations 22 to 36, thereby coordinating the overall operation of the processing module 14.

The particular master control schedule 590 for the illustrated processing system 10 will be described in greater detail later.

II. SPECIFIC DESCRIPTION OF THE PROCESSING MODULE IN THE PREFERRED EMBODIMENTS

The overall operation of the various processing stations and the more specific structural arrangements of the illustrated and preferred embodiments will now be described. The processing stations 22 to 36 will be described in the same general sequence in which they are encountered by a carrier 12 as it proceeds through the processing module 14; namely (1) the carrier dispensing station 22; (2) the sample dispensing station 24; (3) the reagent dispensing station 26; (4) the incubation stations 28 A to I; (5) the washing station 30; (6) the substrate dispensing station 32; (7) the reader station 34; and (8) the carrier disposal station 36.

By way of general layout (as Fig. 1 shows), when viewed from the front, the carrier dispensing station 22 occupies the top center portion of the processing module 14, being positioned between the sample dispensing station 24 and the reagent dispensing station 26.

When viewed from the rear (as Fig. 4 shows), the central hub 100 and shuttle member 20 occupy the approximate center of the interior region of the processing module 14. The washing station 30 and substrate dispensing station 32 occupy the back center region of the interior region. The reader and dump stations occupy one interior side region, while the interior portions of the reagent dispensing station 26 occupy the other interior side region of the processing module 14. The various incubation stations 28 A to I are scattered at various locations around the central hub 100, as just described.

A. The Carrier Dispensing Station

As Figs. 26 to 30 show, the carrier dispensing station 22 includes a storage bin 136 that holds a plurality of test carriers 12 in a vertically stacked arrangement. A hinged door 138 with a clear glass panel (see Fig. 1 also) provides access to the bin 136 from the front of the processing module 14.

By opening the door 138, the test carriers 12 can be loaded by the user into the bin 136 so that the first carrier sidewalls 78A/B face fore-and-aft within the bin 136. As Fig. 27 shows, the upper portion of the bin 136 has a fore-and-aft dimension that is significantly greater than the fore-and-aft dimension of the carrier 12, thereby providing clearance to simplify loading. A front guide bar 142 keeps the carriers 12 stacked within the bin 136 from toppling out when the door 138 is open.

As Fig. 27 also shows, the lower portion of the bin 136 has a reduced fore-and-aft dimension that is only slightly greater than the fore-and-aft dimension of the carrier 12. There, front and rear guide plates 146 contact the rear sidewalls 78A and 78B of the carriers 12 to align the carriers 12 in a vertical direction.

The lower portion of the bin 136 communicates with the hub access 23 for the carrier dispensing station 22 (at the first arcuate position of the shuttle member 20).

As Figs. 26 and 28 to 30 show, a pair of oppositely spaced stops 150 span the lower bin portion 144 in a fore-and-aft direction. A spring 152 biases each stop 150 toward an extended position within the access 23 and projecting into the path of

the vertical stack of carriers 12 (as Fig. 26 shows). The second sidewalls 80A/B of the bottommost carrier 12 in the bin 136 normally rest against these stops 150 to block the release of carriers 12 into the access 23.

The stops 150 are each linked to a solenoid 154 coupled to the control mechanism of the carrier dispensing station 22. Upon receipt of the appropriate control signal, the solenoids 154 operate in tandem to withdraw the stops 150 (as Fig. 28 shows). Upon termination of the control signal, the springs 152 automatically return the stops 150 to their normal extended position (as Fig. 29 shows).

The control mechanism for the shuttle member 20 acts in concert with the control mechanism for the carrier dispensing station 22 to remove test carriers 12 one at a time from the carrier dispensing bin 136.

More particularly, when it is time to remove a test carrier 12, the control module 16 issues the prescribed control command to the shuttle control mechanism. As shown in solid lines in Fig. 28 and in phantom lines in Fig. 31, the shuttle control mechanism moves the shuttle platform 70 into the hub access 23 and upward into contact with the lowermost test carrier 12 in the bin 136. The shuttle platform 70 lifts the lowermost carrier 12 off the stops 150, thereby also lifting the entire stack of carriers 12. The control mechanism for the carrier dispensing station then withdraws the stops 150 (also shown in Fig. 28).

As Fig. 29 shows, with the stops 150 withdrawn, the shuttle platform 70 lowers to move the lowermost carrier 12 below the stops 150. The

stops 150 return to their normally extended position. As Fig. 30 shows, as the shuttle platform 70 further lowers, the bottommost carrier 12 moves into the hub access 23, while the sidewalls 80A/B of the next adjacent carrier 12 are brought to rest against the now extended stops 150.

As shown in solid lines in Fig. 31, the shuttle control mechanism next moves the shuttle platform 70, now carrying the released carrier 12, to the hub access 25 for the sample dispensing station 24, as will be described in the next section.

A first infrared sensor 156 (see Fig. 27) provided at a predetermined level in the upper part of the bin 136 senses when the topmost carrier 12 drops below the level of the sensor 156. When this occurs, a "Reminder: Refill Carrier Bin" message is generated for display to the operator. A second infrared sensor 158 provided at a predetermined level in the lower part of the bin 136 further senses when the topmost carrier 12 drops below the level of the sensor 158. When this occurs, a "Low Carrier Level" message (preferably with an audible alarm) is generated for the operator. Preferably, the control module 16 also prevents further dispensing of carriers 12 until additional carriers 12 are placed into the bin 136 to bring the level of the stack at least above the low limit sensor 158.

B. <u>The Sample Dispensing Station</u>

As Fig. 31 shows, upon removal of a test carrier 12 from the carrier bin 136 and into the associated hub access 23 (as described above), the shuttle control mechanism moves the platform 70 first radially inward (toward the main shuttle frame

56) to move the platform 70 out of the hub access 23, then axially downward, and then radially outward to move the platform 70 (and, with it, the carrier 12) into the hub access 25 for the sample dispensing station 24.

1. **Delivery of the Carrier to the Sample dispensing station 24**

The sample dispensing station 24 includes a pipetting station 162 that, when viewed from the front of the processing module 14 (as Figs. 1 and 32 show), is positioned to the right of the carrier dispensing station 22.

As best shown in Fig. 32, the sample pipetting station 162 itself is spaced away from the hub access 25 of the sample dispensing station 24. An enclosed pathway 164 leads from the hub access 25 to the sample pipetting station 162.

As Fig. 32 shows, a transporter 166 is movable in the pathway 164 between the hub access 25 and the sample pipetting station 162.

The pathway 164 includes the carrier support surface 92 already described. The surface 92 of the pathway 164 includes a spaced pair of grooves 96 like those shown in Fig. 12 that engage the flanged bottom edges 86A/B of the received carrier 12.

As Fig. 32 shows, the transporter 166 includes an outreached finger 168 that engages an adjacent sidewall 80B of the carrier 12 as the carrier 12 is placed upon the support surface 92.

The transporter 166 is carried along an axial screw 170 driven by a stepper motor 172. The stepper motor 172 is actuated by the control mechanism for the sample dispensing station 24. The

stepper motor 172 rotates the screw 170 to advance the transporter 166 along the screw 170 either toward the sample pipetting station 162 or back toward the hub access 25. When engaged by the finger 168, the transporter 166 moves the carrier 12 within the grooves 96 when the stepper motor 172 operates.

The shuttle control mechanism acts in concert with the control mechanism of the sample dispensing station 24 to move the transporter 166 into the proper position within the hub access 25 to engage the carrier 12 with the finger 168 as the shuttle platform 70 arrives and deposits the carrier 12 in the hub access 25. Then, the control mechanism of the sample dispensing station 24 operates the stepper motor 172 to move the transporter 166 (and, with it, the carrier 12) to the sample pipetting station 162 (as shown by arrows in Fig. 32).

The transporter 166 frees the shuttle member 20 to perform other tasks as fluid samples are dispensed into the carrier 12.

In the illustrated and preferred embodiment (as Fig. 32 also shows), the environmental control system 52 includes an electrical resistance heater 174 located directly beneath the pathway 164 that leads between the hub access 25 and the sample pipetting station 162. An associated thermistor 176 maintains the heater at a desired temperature, which in the illustrated embodiment is in the range of between 30 and 45 degrees centigrade. A heated dropped ceiling element 108 with associated thermistor 176 is also provided. The test carrier 12 thereby continues to be exposed to a constant, desired temperature condition as it receives source

specimen. As before described, foam 106 insulates the interior regions of the work station 24.

2. Delivery of Source Specimens to the Sample Dispensing Station

As Fig. 33 shows, the sample dispensing station 24 also includes a sample delivery assembly 178 that transports one or more specimen source containers to and from the sample pipetting station 162.

When viewed from the front of the processing module 14 (as Fig. 33 shows), the sample delivery assembly 178 is positioned below and on either side of the sample pipetting station 162. The delivery assembly 178 includes a specimen supply mechanism 180 (to the right of the sample pipetting station 162) and a specimen discharge mechanism 182 (to the left of the sample pipetting station 162). The sample pipetting station 162 is positioned in the path between the two mechanisms 180 and 182.

The specimen supply and discharge mechanisms 180 and 182 accommodate one or more racks 184 of test tubes 186 (also shown in Fig. 35). Each tube 186 contains a specimen of source fluid to be analyzed by the processing module 14. In the illustrated embodiment, the source fluid is blood plasma or serum.

The racks 184 are conveyed, one at a time, from the supply mechanism 180, into and through the sample pipetting station 162. There, fluid from the test tubes 186 is transferred to a waiting test carrier 12. The racks 184 then move to the discharge mechanism 182.

a. Source Specimen Racks

As Fig. 35 shows, each source specimen rack 184 can carry a plurality of test tubes 186. In the illustrated embodiment, the tubes 186 are arranged within each rack 184 in a straight row. In the illustrated embodiment, in which a single carrier 12 can handle up to twelve source specimens, each rack 184 can carry upwards to twelve test tubes 186. Thus, each rack 184 contains enough source specimens for one carrier 12.

In the illustrated embodiment, the specimen supply mechanism can handle upwards to ten racks 184 at a time, thereby supplying enough source containers to fill ten test carriers 12.

Each rack 184 can be variously constructed. In the illustrated embodiment (see Figs. 35 and 36), each rack 184 is made of lightweight, molded plastic that is autoclavable for reuse. The rack 184 includes a base portion 188, open at the bottom, containing a series of generally equally spaced ribs 190. The ribs 190 subdivide the base portion 188 into interior pockets 192, with the number of pockets 192 equal to the number of test tubes 186 that can be carried on the rack 184.

The rack 184 includes upstanding sidewalls 194 that form an interior area, open at the top. One sidewall 194 is cut open at prescribed intervals to form a series of windows 196. Each window 196 is generally placed between two adjacent ribs 190 in the base portion 188, so that each test tube 186 can be placed in the rack 184 with its label 187 facing out of the corresponding window 196.

In the illustrated embodiment, an outwardly biased spring 198 (see Fig. 35) urges each test tube 186 toward its corresponding window 196, keeping

each test tube 186 stationary within the rack 184 with its label 187 exposed as it is conveyed through the sample pipetting station 162. The flexible spring 198 also allows the user to place test tubes 186 of differing diameters within the rack 184.

As Fig. 28 shows, each rack 184 also includes a label 185 with indicia that uniquely identifies it. Each test tube 186 within the rack 184 also includes an individual label 187 with indicia that uniquely identifies the source of its contents. In this way, a record can be established that correlates each rack 184 to a given carrier 12 and each well 18 within a given carrier 12 to the source of its contents and the particular assay that is performed. As will be described in greater detail later, this record is preferably automatically generated by the system 10.

b. Source Specimen Supply and Discharge Mechanisms

As best shown in Fig. 33, the specimen supply mechanism 180 includes a ramp 200 to hold the racks 184 in line while awaiting delivery to the sample pipetting station 162. A first conveyor 202 sequentially delivers the racks 184 on the ramp 200 to the sample pipetting station 162.

While various constructions are possible, in the illustrated embodiment (as Fig. 33 shows), the first conveyor 202 includes a pair of pusher bars 204 that are movable in tandem within trackways 206 formed in the ramp 200. Each pusher bar 204 is linked to a belt 208 that extends between a drive pulley 210 and an idler pulley 212. Each drive pulley 210 is in turn attached to a common drive shaft 214 that is connected by another belt drive

216 to a stepper motor 218.

The control mechanism of the sample dispensing station 24 actuates the stepper motor 218 to advance the pusher bars 204 in tandem through the trackways 206. The pusher bars 204 bear against the forwardmost rack 184 present in the ramp 200, sliding it and all the other racks 184 behind it in a group toward the sample pipetting station 162. Each time the stepper motor 218 operates, it advances the pusher bars 204 for a discrete distance so that, during each cycle, one rack 184 is delivered to the sample pipetting station 162.

In the illustrated embodiment (as Fig. 36 shows), a magnet 220 is attached to the bottom of each rack 184. A magnetic "Hall Effect" sensor 222 is provided in the region of the sample pipetting station 162 where the rack 184 is delivered (as Fig. 26 shows). This sensor 222 detects the presence of the magnet 220, thereby detecting the delivery of a rack 184 to the ramp 224 leading to the sample pipetting station 162. Upon sensing the arrival of the rack 184, a second conveyor 226 operates to further advance the rack 184 along the ramp 224.

While various constructions are possible, in the illustrated embodiment (as Fig. 38 shows), the second conveyor 226 includes a pair of pusher bars 228 that move in tandem in a rectilinear path above and below a trackway 230 formed on the ramp 224. The pusher bars 228 are spaced apart on an eccentric link 232 at a distance equal to the spacing between adjacent ribs 190 in the bottom portion 188 of the rack 184, or some multiple thereof. The eccentric link 232 is pivotally attached to two spaced apart drive gears 234A/B that are, in turn, coupled to a stepper motor 236 for

common rotation by two intermediate gears 238A/B.

The control mechanism for the sample dispensing station 24 operates the stepper motor 236 in a cyclic fashion, during which the drive gears 234 A/B rotate one complete revolution in a counterclockwise direction.

The cycle begins with the pusher bars 228 located in a first position withdrawn below the trackway 230. As the drive gears 234A/B rotate in a counterclockwise direction for about ninety degrees, the eccentrically linked pusher bars 228 move in tandem in a vertically upward path protruding above the trackway 230. As Fig. 30 shows, the pusher bars 228 engage two spaced-apart ribs 190 on the bottom of the rack 184. As the drive gears 234A/B continue to rotate another ninety degrees, the pusher bars 228 move in a horizontal path above the trackway 230 (from right to left in Fig. 37) a distance that corresponds to the distance between adjacent ribs 190 on the bottom of the rack 184. The engaged rack 184 thereby advances on the ramp 224 a distance equal to the spacing between adjacent test tubes.

As the drive gears 234A/B rotate the remaining one hundred and eighty degrees, the linked pusher bars 228 move in tandem in a vertically downward path out of the trackway 230 and, while still withdrawn from the trackway 230, move back to the first position, ready for another cycle.

During each cycle of the stepper motor 236, the second conveyor advances the rack 184 on the ramp 224 in stepwise fashion under the sample pipetting station 162 one test tube 186 at a time toward the sample discharge mechanism.

As Fig. 34 shows, an infrared scanner 240 sequentially reads the labels 185/187 on the rack

184 and each test tube 186 as they advance through the sample pipetting station 162. The scanner 240 transmits the information to the main control module 16, where a complete data base is developed and maintained that serializes each rack 184 to a given carrier 12 and each well 18 within a given carrier 12 to the source of its contents and the particular assay that is performed.

As Fig. 33 also shows, the sample discharge mechanism 182 includes yet another ramp 242 to receive the racks 184 as they exit the sample pipetting station 162. A third conveyor 244 advances the racks 184 on the ramp 242 away from the sample pipetting station 162.

Various constructions are possible. In the illustrated embodiment (shown in Fig. 38), the third conveyor 244 includes a pair of pusher bars 246A/B movable in tandem in slots 248 formed in the ramp 242. A link 250 joins the pusher bars 246A/B. One pusher bar 246A is carried on an axial screw 252 coupled to a stepper motor 254 by a belt drive 256. The other pusher bar 246B is movable along a rod (not shown) in tandem with the pusher bar 246A. The control mechanism of the sample dispensing station 24 actuates the stepper motor 254 to operate the pusher bars 246A/B in cyclic fashion.

The cycle begins with the pusher bars 246A/B in a first position (shown in solid lines in Fig. 38). A rack 184 moves along a guide 260 by the second conveyor 226 from the sample pipetting station 162 into an eject position next to the pusher bars 246A/B. The control mechanism actuates the stepper motor 254. The stepper motor 254 rotates the axial screw 252 to advance the pusher bars 246A/B from their rest position forwardly (from

right to left in Fig. 38) a fixed distance to a second position (shown in phantom lines in Fig. 38). The fixed distance is larger than the width of a rack 184. The advancing pusher bars 246A/B bear against the adjacent rack 184, sliding it and all other racks 184 positioned in front of it as a group away from the sample pipetting station 162.

Upon reaching the second position, the stepper motor 254 reverses the rotation of the axial screw 252 to return the pusher bars 246A/B rearwardly (from left to right in Fig. 31) back to their rest position. The cycle ends, awaiting the delivery of another rack 184 into the eject position.

3. Delivery of Source Specimen to the Carrier

As best shown in Figs. 32 and 39, the pathway 164 leading from the access 25 to the sample pipetting station 162 extends below a panel 262 having two spaced apart slots 264 and 266 in the region of the sample pipetting station 162. The centerlines of the slots 264 and 266 are generally parallel and extend in a fore-and-aft direction (as viewed from the front of the processing module 14). The slots 264 and 266 extend in axial (elongated) length a distance necessary to span the number of wells 18 located in each column on the carrier 12 (which, in the illustrated embodiment, is a distance of eight wells 18). The centerlines of the slots 264 and 266 are spaced a predetermined distance apart conforming to the spacing between the centers of adjacent test tubes 186 on the rack 184, or some multiple thereof.

The control mechanism operates the

transporter 166 to move the carrier 12 beneath the panel 262 to position a selected column in the desired alignment with one slot 264 or 266, following a predetermined sequence that will be described in great detail later.

When viewed from the front of the processing module 14, the ramp 224 on which the rack 184 advances through the sample pipetting station 162 is located in front of the slotted panel 262 (as Fig. 39 shows).

a. The Sample Pipette Subassembly

Still referring principally to Fig. 39, the sample dispensing station 24 includes a sample pipette subassembly 268 that is movable between the pipetting station ramp 224 and the slotted panel 262 to transfer source fluid from the test tubes 186 to the test wells 18 of the carrier 12 exposed through the slots 264 and 266. The control mechanism of the sample dispensing station 24 coordinates these fluid transfer operations, subject to the overall direction of the control module 16.

The sample pipette subassembly 268 includes a pair of side-by-side, stationary booms 270 and 272 that span the pipetting station ramp 224 and the slotted panel 262. One boom 270 extends from the ramp 224 axially over the one slot 264, while the other boom 272 extends from the ramp 224 axially over the other slot 266. The subassembly 268 also includes first and second pipettes 274 and 276, one mounted on each boom 270 and 272, respectively. Each pipette 274 and 276 includes a pipetter probe 275 and 277, respectively, through which fluid is transferred.

Each pipette 274 and 276 is attached to a

carriage 278 and 280 on its respective boom 270 and 272. Each carriage 278 and 280 is independently movable on its associated boom 270 and 272 in a horizontal direction (which is fore-and-aft in Fig. 39) between the associated slots 264 and 266 and the ramp 224. A carriage drive belt 282 driven by a carriage stepper motor 284 operated by the control mechanism, moves each carriage 278/280 horizontally on its respective boom 270/272.

The first and second pipettes 274/276 are each also independently movable in a vertical direction (up and down) upon its respective boom 270/272 (as is also shown in Fig. 25). A conventional jack screw 286 driven by a stepper motor (not shown) operated by the control mechanism, moves each pipette 274/276 vertically on its respective boom 270/272.

The control mechanism selectively actuates each carriage stepper motor 284 to insure accurate movement of the associated pipette 274/276 in a horizontal direction, to align a selected probe 275/277 with the centerline of a desired test tube 186 or carrier well 18. The control mechanism also selectively actuates each jack screw stepper motor to lower and raise the associated probes 275/277 axially of the aligned centerline of the test tube 186 or carrier well 18.

The sample pipette subassembly 268 further includes a washing well 290/292, one for each probe 275/277 (see Fig. 32). In the illustrated embodiment, the washing wells 290/292 are located in the path of movement of the associated probe 275/277 between the ramp 224 and the associated slot 264/266. The control mechanism selectively actuates the carriage stepper motors 284 and jack screw

stepper motors to position a selected probe 275/277 with respect to its washing well 290/292 at the proper time. There, a washing fluid is conveyed through the probe 275/277 and into the well 290/292, as will be described in greater detail later.

Fig. 23 shows the representative fluid delivery circuit 40 for the sample dispensing station 24. As there shown, the sample pipette subassembly 268 includes three syringe pumps 294, 296, and 298, each with an associated valve 295, 297, and 299, respectively, for delivering fluids to the first and second pipettes 274/276. A separate high volume rotary wash pump 300 conveys wash fluid through the first pipette 274.

The first syringe pump 294 communicates with the first pipette 274 to convey source fluid into and out of the associated probe 275. The second and third syringe pumps 296 and 298 communicate with the second pipette 276. These pumps 296 and 298 act in concert to convey source fluid (via the second pump 296) and diluent (via the third pump 298) into and out of the probe 277 of the second pipette 276.

As Figs. 40 and 41 show, each syringe pump 294/296/298 includes a pump chamber 302 having an outlet 304 and a pump piston 306 movable within the chamber 302 toward and away from the outlet 304. Movement of the pump piston 306 away from the outlet 304 draws (or aspirates) fluid into the associated probe 275/277, while movement of the pump piston 306 toward the outlet 304 expels fluid from the associated probe 275/277.

The pump piston 306 is attached to an actuator 308 that is carried on an axial screw 310 and guide bar 312. A stepper motor 314

independently rotates each axial screw 310 to advance the actuator 308 either axially up or down the screw 310, thereby moving the attached pump piston 306 toward or away from the chamber outlet 304. The control mechanism selectively operates the desired stepper motor 314 to coordinate the conveyance of fluid by the probes 275/277.

As shown in Fig. 23, the washing wells 290 and 292 communicate with the waste fluid circuit 46, which is itself shown in Fig. 24.

4. Sequence of Operation

In the illustrated embodiment, the control mechanism for the sample dispensing station 24 fills the carrier 12 following a prescribed sequence of steps (which Fig. 42 shows diagrammatically).

In general, the sequence employs the first probe 275 to transfer undiluted (or so-called "neet") fluid between the source (i.e., the test tubes 186) and predesignated test wells 18, while also continuously washing the second probe 277. The sequence then washes the first probe 275 while simultaneously employing the second probe 277 to prepare diluted samples of the source fluid by drawing upon the fluid present in one well 18 previously filled by the first probe 275, adding to it a predetermined amount of diluent, and then discharging the diluted sample into one or more additional test wells 18.

This division of tasks allows the first probe 275 to be optimized for relatively high volume transfer of fluid (per unit of time) while optimizing the second probe 277 for relatively smaller volume fluid transfer to make precise dilutions of the source fluid. In the illustrated

embodiment, the first probe 275 has an interior diameter of about .024 inch, whereas the second probe 277 has a smaller interior diameter of .010 inch. The separate high volume wash pump 300 is provided because of the larger fluid handling capacity of the first probe 275.

The sample dispensing sequence begins by conveying the first carrier 12 to be filled from the carrier dispensing station 22 to the access site 25 in the manner previously described. From there, the transporter 166 moves the carrier 12 to the sample pipetting station 162 and positions the carrier 12 so that the eight wells 18 of the first column (i.e., the entire first test sector) are axially aligned under the first slot 264.

During the same general period, the first and second conveyors 202 and 226 convey to the sample pipetting station 162 a rack 184 holding the test tube 186 of the first source fluid to be analyzed. The rack 184 is positioned so that the centerline of the test tube 186 containing the first source fluid to be analyzed is positioned under the first boom 270.

In the illustrated embodiment, an infrared tube detector 326 (see Fig. 34) senses the presence of the test tube 186 when located in its proper position beneath the first boom 270. An error signal is generated when the test tube 186 is either missing or otherwise out of its proper position.

During this pre-positioning period, the first probe 275 is located within its washing well 290.

As Figs. 43 to 45 show, the washing well 290 is divided into three chambers 328, 330, and 332. An outlet 334 extends from the first chamber

328. The vacuum pump 316 of the waste fluid system 46 communicates with the outlet 334 to draw wash solution from the chamber 328.

An inlet 336 in the third chamber 332 conveys wash fluid from reservoir R6 through a wash pump 338, which in the illustrated embodiment is located beneath the ramp 242 (as shown in Fig. 23 and in phantom lines in Fig. 33).

In use, the probe 275 is first placed into the first chamber 328 (as Fig. 44 shows). Solution is pumped from reservoir R2 (via the high volume washing pump 300) to flush material from the interior of the first probe 275.

Next, the probe 275 is placed into the second chamber 330 (as Fig. 45 shows). Solution is again pumped from reservoir R2 via the high volume pump 300 through the probe 275. This solution circulates vigorously within the closed second chamber about the exterior of the probe 275, spilling over into the first chamber 328 for discharge through the outlet 334. This washes the exterior region of the probe 275.

Finally, the probe 275 is placed into the third chamber 332 (as Fig. 46 shows). Fluid is continuously circulated through the inlet 336 about the probe, spilling over into the first chamber 328 for discharge through the outlet 334. Here the probe 275 soaks until time of use.

The control module 16 soaks the probe 275 during each sample dispensing operation. The control module 16 also preferable includes a user actuated "Rest" command that moves the probe 275 to its soak position (i.e., within the third chamber 332) during periods when the system 10 is temporarily shut down for maintenance or during

breaks in processing activities.

The construction of the well 292 is identical to well 290. The sequence of washing and soaking the probe 277 is also identical to the one just described, except that the wash pump 300 is not needed used to convey wash fluid through the probe 277. Because the second probe 277 has a smaller interior diameter, operation of the syringe pump 298 provides sufficient washing effect.

As the test carrier 12 and rack 184 are moving into position, operation of the washing pump 300 stops. In the illustrated embodiment, the first syringe pump 294 operates (by moving the piston 306 down) to capture a predetermined small volume of buffered solution in the associated pump chamber 302. This small volume of buffered solution, captured within the syringe pump 294 for the first probe 275 after its washing cycle, is later used to form the first diluted sample of the source specimen. However, in other arrangements, this initial step can be eliminated.

The first pipette 274 then operates to lift the first probe 275 from the washing well 290 and to move it horizontally on the boom 270 into registration over the awaiting, prepositioned test tube 186. The first probe 275 then lowers into the source fluid in the test tube 186.

The first syringe pump 294 operates to lower the pump piston 306 and draw a volume of source fluid into the first probe 275 (as Step A in Fig. 42 shows). The probe 275 (now containing the volume of source fluid) lifts from the test tube 186.

The first probe 275 then moves horizontally on the boom 270 into an initialized position in

registration over the first test well 18 of the first test column, occupying Row 1 of Column 1 of the carrier 12, or test well (R1, C1). The first probe 275 then lowers into the test well (R1, C1) by actuating the jack screw stepper motor 288.

The first syringe pump 294 now operates to raise the pump piston 306 and expel a prescribed aliquot of neet (undiluted) source fluid through the first probe 275 and into the first well (R1, C1) (as Step B in Fig. 42 shows).

The first probe 275 then raises from the well (R1, C1). The transporter 166 operates to now move the carrier 12 one column width (to the left in Fig. 35) to align the test wells 18 of the second column with the first slot 264, keeping the probe 275 initialized with respect to the first test row. The first probe 275 then lowers into the second test well 18 for the first test row, or test well (R1, C2). The first syringe pump 294 again operates (raising the pump piston 306 further) to expel another prescribed aliquot of neet (undiluted) source fluid through the first probe 275 and into the well (R1, C2) (as Step C in Fig. 42 shows). The probe 275 again raises.

The test wells (R1, C1) and (R1, C2) now each contains a neet (undiluted) sample of the source fluid, as required for the HBs (Ag) and HBc (Ag) assays that are to be performed, respectively, on these samples in these processing sectors C1 and C2 (as Fig. 10 shows).

The transporter 166 next operates to advance the carrier 12 another column width to the left, still keeping the now-lifted first probe 275 initialized with respect to the first test row, to bring the test wells 18 of third column into

alignment with the slot 264. The initialized probe 275 then lowers into the third test well 18 for the first test row, or test well (R1, C3). The first syringe pump 294 again actuates to expel the remaining the source fluid from the probe 275 and into the test well (R1, C3) (as Step D in Fig. 42 shows). In the illustrated embodiment, with this final stroke, the captured volume of buffered solution is also expelled from the pump chamber 302 and into the test well 18, thereby forming the first dilution of the source fluid, as required for the ALT assay to be performed in this test sector C3 (see Fig. 10).

As Steps A to D in Fig. 42 show, while the first probe 275 operates to convey samples into the three test wells 18 (i.e., columns 1 to 3) of the selected test row, the second probe 277 soaks within its washing well 292, and the second syringe pump 277 continuously conveys buffered solution to wash the second probe 277.

Preferably, the source fluid is heated to the temperature of the test carrier 12 prior to entering a test well 18 of the carrier 12. While this result can be obtained by various means, in the illustrated embodiment (as Fig. 47 shows), the environmental control system 52 includes a length of resistance wire wrapped about the tip of the first probe 275 to thereby form an electrical resistance heater 346. A thermistor 348 coupled to the probe heater 346 maintains a constant temperature of in the range of 30 and 45 degrees centigrade, the same temperature to which the pathway 164 is heated. The heater and thermistor 346 and 348 are sealed within a shell of plastic 350 that encapsulates the first probe 275.

In the illustrated and preferred embodiment (as Fig. 47 also shows), the control mechanism for the sample dispensing station 24 includes a liquid level sensor 352 that is also carried on the tip of the first probe 275. The sensor 352 extends a predetermined distance outside the plastic shell 350 and is spaced away from the tip of the probe 275. The conduction of electricity between the sensor 352 and the probe 275 (as will occur when both come into contact with fluid) generates a signal that terminates the operation of the first syringe pump 294. The sensor 352, in combination with the jack screw arrangement, assures that the first probe 275 consistently conveys precise aliquots of source fluid to the test wells 18.

After the aliquot is conveyed to the third test well (R1, C3), the first probe 275 lifts and moved horizontally away from the slot 264 and into registration over its washing well 290. The first probe 275 lowers into its washing well 290. Meanwhile, the flow of washing fluid to the second probe 277 terminates, and the flow of washing fluid to the first probe 275 begins by operation of the washing pump 300.

The transporter 166 moves the test carrier 12 six column widths to the right (as viewed in Fig. 35), bringing the third column of wells (C3) into alignment with the second slot 266 (as Step E in Fig. 35 shows).

The second probe 277 lifts from its washing well 292 and moved horizontally on its boom 272 to the second slot 266. The second probe 277 is located in an initialized position over the second slot 266 in registration with the first test row of the third column; that is, test well (R1, C3)].

Once initialized, the second probe 277 lowers into the first diluted sample of fluid that was conveyed previously into the well (R1, C3) by the first probe 275. The second syringe pump 296 operates in the manner previously described to draw a prescribed volume of fluid from this well (R1, C3) into the probe 277, while the third syringe pump 298 operates to draw a volume of buffered solution into the associated pump chamber 302 (as Step E in Fig. 42 shows).

The second probe 277 raises, while being kept in its initialized position, and the transporter 166 moves the wells 18 in the fourth column into alignment with the second slot 266. The second probe 277 then lowers into the fourth test well 18 in the first test row; that is, test well (R1, C4). An aliquot of fluid is conveyed through the second probe 277 into the well (R1, C4) by the operation of the second syringe pump 296 (as Step F in Fig. 42 shows). At the same time, the third syringe pump 298 operates to introduce a prescribed amount of buffered solution through the second probe 277, thereby forming a second dilution of the sample for the HIV-1 assay that is to be performed in processing sector C4 (see Fig. 10).

The sequence repeats: the second probe 277 again raises, the carrier 12 again moves over one column. The second probe 277 lowers to convey the first dilution of source fluid in succession into the fifth and sixth test wells 18 for the first test row, i. e., test wells (R1, C5) and (R1, C6), each time adding further diluent by operation of the third syringe pump 298 to further dilute the conveyed sample (as Steps G and H in Fig. 42 shows). The third and forth diluted samples are thereby

formed for the HTIV-1 and TPA assays that are to be performed in processing sectors C5 and C6, respectively.

Once the dilution sequence is complete, the second probe 277 lifts and moves to its washing well 292, and the third syringe pump 298 conveys buffered solution to wash the second probe 277. At the same time, conveyance of washing fluid to the first probe 275 stops. The first probe 275 lifts out of its washing well 290 and resumes another delivery sequence while washing fluid is conveyed to the second probe 277.

The delivery and dilution sequence as just described repeats for the second through the sixth source specimens, during which the test wells (C1 to C6) in the second and subsequent test rows (R2 to R6) are filled. In beginning each sequence, the carrier 12 is repositioned by the transporter 166 to bring the test wells 18 of the first column back into alignment with the first slot 264. At the same time, the rack 184 sequences one step to the left to bring the test tube 186 containing the next source specimen to be analyzed into alignment with the first boom 270. The position of the first probe 275 is reinitialized this time to convey source fluid from the test tube 186 to the first test well 18 in the next test row; i.e., at the first column of the second test row for the second source specimen, i.e., test well (R2, C1); at the first column for the third test row for the third source specimen, i.e., test well (R3, C1); at the first column for the fourth test row for the fourth source specimen, i.e., test well (R4, C1); and so on for the first six source specimens.

For the seventh and remaining source

specimens, the position of the first probe 175 is again reinitialized to convey source fluid from the seventh and subsequent test tubes 186 beginning at the seventh column of the first and subsequent test rows; that is, at well (R1, C7) for the seventh source specimen; at well (R2, C7) for the eight source specimen; at well (R3, C7) for the eighth source specimen; and so on.

By using two individually operated probes 275 and 277, one filling while the other one washes, the sample dispensing station 24 minimizes lost time due to washing and transport of the probes. Also, only the first probe 277 is directly exposed to neet (undiluted) fluid. Also, because of the dilution technique used employing the second probe 277, the source well for the dilution process also ultimately serves as a test site on the carrier 12.

When the carrier 12 present at the sample pipetting station 162 has received all the source specimens it should receive, the control mechanism for the sample dispensing station 24 actuates the transporter 166. The transporter 166 moves the carrier 12 (now filled with source specimens) from the sample pipetting station 162 back to the hub access 25.

Throughout the above described sequence, the control module 16 has been periodically sending status inquiries to the control mechanism of the sample dispensing station 24. While samples of source fluid are being conveyed to the test carrier 12, the control mechanism responds with a "Busy" signal. When fluid transfer operations stop, and the test carrier 12 has been returned to the hub access 25, the control mechanism returns a "Not Busy" signal to the status inquiry of the control

module 16.

Upon receipt of the "Not Busy" signal, the main control module 16 sends an appropriate command signal to the control mechanism for the shuttle member 20, instructing the control mechanism to send the shuttle member 20 to the hub access 25 to pick up the awaiting test carrier 12. The command signal also instructs the control mechanism for the shuttle member 20 to transport the carrier 12 to the next work station, which in the illustrated embodiment is the reagent dispensing station 26.

C. **The Reagent Dispensing Station**

When viewed from the front (as Fig. 1 shows), the reagent dispensing station 26 occupies the left hand portion of the processing module 14 above the compartment 44 where the bulk fluid storage containers 42 and reservoirs 43 are stored.

The hub access 27 for the reagent dispensing station 26 is positioned in the second arcuate position A2 of the shuttle member 20. This hub access 27 is arcuately spaced ninety degrees from the hub accesses 23 and 25 for the carrier and sample dispensing stations 22 and 24, just described (as Figs. 7 and 8). In the illustrated embodiment, the hub access 27 is generally in the same horizontal plane as the hub access 23 (see Fig. 8).

1. **Delivery of the Carrier to the Reagent Dispensing Station**

Once the proper command signal is received from the control module 16, the shuttle member 20 transports the carrier 12 from the hub access 25 to the hub access 27 in response to commands issued by the shuttle control mechanism.

In response to these commands, the shuttle member 20 rotates the platform 70 to the first arcuate position to pick up the carrier 12 at the hub access 25. When in this arcuate position, the platform 70 moves radially outward (away from the main shuttle frame 56) into the hub access 25, while its orientation is adjusted axially up or down to enter the prescribed pick up position below the cutout portion 94 of the access (as generally shown in Fig. 14). The platform 70 next raises to engage the carrier 12 in the manner previously described. The platform 70 then moves radially inward (toward the main shuttle frame 56) out of the hub access 25, and the shuttle member 20 rotates to the second arcuate position. The platform 70 then moves radially outward, with appropriate axial up or down adjustments, to move the engaged carrier 12 into its drop-off position in the hub access 27 for the reagent dispensing station 26.

As Fig. 48 shows, the reagent dispensing station 26 includes a reagent pipetting station 354 that includes a supporting work surface 92 for receiving the carrier 12. The work surface 92 has a cutout portion 94 in the hub access 27. As with the cutout portion 94 associated with the sample dispensing station 24, the shuttle platform 70 enters this cutout portion 94 with the carrier 12 at a drop-off position above the plane of the work surface 92. The platform 70 then lowers through the cutout portion 94 to lift the carrier 12 off the platform 70 and into the work surface 92.

Also like the work surface 92 of the sample dispensing station 24, the work surface 92 of the reagent dispensing station 26 includes a spaced pair of transverse grooves 96 (as Fig. 48 shows). The

grooves 96 capture the flanged edges 86A/B of the carrier 12 as the carrier 12 is placed onto the work surface 92. The reagent pipetting station 354 also includes its own dedicated transporter 356 that is transversely movable in the work surface 92 axially along one groove 96.

As Fig. 48 shows, the transporter 356 is carried by an axial screw 358 driven by a stepper motor 360 operated by the control mechanism for the reagent dispensing station 26. The stepper motor 360 rotates the screw 358 either clockwise or counterclockwise to advance the transporter 356 in opposite linear direction along the screw 358 (either to the left or to the right in Fig. 48).

The transporter 356 is specifically configured to mate with the keyway 82B on the rearward sidewall 78B of the carrier 12. The shuttle control mechanism acts in concert with the control mechanism of the sample dispensing station 24 to move the transporter 356 (via operation of the stepper motor 360) into the proper position within the hub access 27 to properly engage the carrier keyway 82B as the shuttle platform 70 arrives and deposits the carrier 12 in the hub access 27. Subsequent actuation of the stepper motor 360 moves the carrier 12 in common with the transporter 356 within the transverse grooves 96 on the work surface 92.

The shuttle member 20 is thereby free to perform other tasks while reagent is dispensed.

In the illustrated and preferred embodiment (as Fig. 48 shows), the environmental control system 52 includes one or more electrical resistance heaters 362 located both above and beneath the work surface 92 of the reagent pipetting station 354. An

associated thermistor (not shown) maintains the heaters 362 at a desired temperature, which in the illustrated embodiment is in the range of between 30 and 45 degrees centigrade. The test carrier 12 thereby continues to be exposed to the same constant temperature condition while at the reagent dispensing station 26.

2. Delivery of Reagent to the Reagent dispensing Station

As shown in Figs. 39 to 41, the reagent dispensing station 26 includes a reagent supply subassembly 366. The reagent supply subassembly 366 includes a reagent storage chamber 368 that houses a reagent carrier 370 (see Fig. 49 also). The reagent carrier 370 includes a series of storage bins 372 into which a plurality of reagent vials 374 have been loaded by the user. The reagent carrier 370 transports the bins 372 containing the reagent vials 374 to a reagent supply station 376, which is located above the reagent storage chamber 368 and next to the reagent pipetting station 354.

When viewed from the rear of the processing module 14 (as Fig. 48 does), the reagent storage chamber 368 and the reagent supply station 376 are situated one above the other directly to the right of the reagent pipetting station 354, where the test carrier 12 is delivered.

a. The Reagent Vials and Packs

In the illustrated embodiment (as Figs. 50 and 52 show), each reagent vial 374 is made from relatively inexpensive, inert plastic material by conventional plastic molding techniques.

Each vial 374 contains the additive

materials, such as reagent, buffer, enzyme label, or suspension of solid phase particles, that are to be used with a given assay process. Each vial 374 is intended to be removed from the carrier mechanism and discarded after its supply of fluid is depleted. An access door 386 (see Figs. 1 and 53) that can be opened and closed by the user from the front of the processing module 14 provides access to the interior of the reagent storage chamber 368.

Since a given analytical procedure often requires the addition of more than a one type of additive material, the vials 374 include means 390 for coupling two or more vials 374 together in a predetermined fashion to create integrated reagent packs 388. A given reagent pack 388 (shown in Figs. 51 to 53) contains all the additive materials required for a reagent addition procedure for a given assay.

As Fig. 48 shows, the integrated packs 388 are carried in the bins 372 transported by the reagent carrier 370. A given carrier bin or bins 372 can thus be dedicated to supply the additive materials required for a given analytical procedure.

In the illustrated and preferred embodiment, the reagent carrier 370 includes an array of bins 372 to contain an adequate supply of additive materials for a given analytical procedure, as well as support many different analytical procedures at the common reagent pipetting station 354.

The coupling means 390 for creating the reagent packs 388 can be variously constructed. In the illustrated embodiment, the coupling means 390 is configured to assure the proper placement of a given vial 374 within a reagent pack 388.

The coupling means 390 includes a holder 392 having openings 394, each of which can be snap-fitted about the neck a vial 374. In the illustrated embodiment (as Fig. 51 shows), the typical reagent pack 388 contains three vials 374. This reagent pack 388 has two end vials 374 A/B and one middle vial 374C.

In this arrangement, the holder 392 has one end 393 with two generally rounded corners and an opposite end 395 with one rounded corner cut off. The rounded corners interfere with the hub 410A/B of the reagent carrier 370, preventing placement of a reagent pack 388 within the bins 374 with the holder end 393 facing the hub 410A/B. To fit a reagent pack 388 within the bins 374, the user must orient the holder with the rounded off hold end 395 facing the hub 410A/B, as Figs. 52 and 53 show.

b. <u>The Reagent Carrier Bins</u>

The storage bins 372 are joined in integral groups of three (as Fig. 49 shows), each three-bin group thereby accommodating a three-vial reagent pack.

As Fig. 49 shows, the reagent carrier 370 includes a center carousel 406 having a drive belt 408 on which the three-bin groups are attached. The drive belt 408 rotates about two hubs 410A/B in response to a stepper motor 412 actuated by the control mechanism for the reagent dispensing station 26.

The rotation of the carousel 406 carries the three-bin groups in a generally elliptical path within the reagent storage chamber 368 that, at one point, extends beneath the reagent supply station 376. By starting and stopping the rotation of the

carousel 406 in a controlled fashion, selected bin groups can be situated beneath the reagent supply station 376.

The supply station 376 includes a two adjacent access sites 414 and 416 for drawing fluids from a bin group situated beneath the station 376. Each site 414 and 416 includes three access openings 414A/B/C and 416A/B/C (see Figs. 48 and 49). Each access opening A/B/C registers with the mouth 384 of one vial 374 contained in the particular bin group located beneath the supply station 376.

c. Storage of Solid Phase Paramagnetic Particles

In the illustrated embodiment, the assays employ solid phase paramagnetic particles 422 as binding sites. The particles are delivered to the designated test wells 18 at the reagent dispensing station 26.

In this arrangement, a selected reagent vial 374 of the reagent pack 388 carries the paramagnetic particles 422 in fluid suspension. In the illustrated embodiment (as Fig. 48 shows), the end vial 374A that occupies the outermost storage bin 372 contains the suspension of paramagnetic particles 422. This is the vial 374A that is closest to the rounded corner end 393 of the vial holder 392.

The paramagnetic particles 422 can settle during storage into the bottom of the storage vial 374A. For this reason, the reagent dispensing station 26 includes means 424 for stirring the paramagnetic particles 422 into suspension prior to being delivered to the test carrier 12.

In the illustrated embodiment (as Figs. 48

and 51 show), the vial 374A containing the paramagnetic particles 422 includes an interior stir rod 426. The stir rod 426 is made of a paramagnetic material having a low magnetic remanence. In the illustrated and preferred embodiment, an inert plastic material encapsulates the paramagnetic material of the stir rod 426.

The stir rod 426 is carried loose within the vial 374A, so that it is free to move within the vial 374A in response to external forces. Still, the stir rod 426 has sufficient weight to sink to the bottom of the fluid in which the paramagnetic particles 422 are suspended. Because the stir rod 426 lacks resident magnetism, the suspended particles 422 are not magnetically attracted or repelled by the stir rod 426.

The reagent dispensing station 26 further includes a stirring stepper motor 428 (see Fig. 39) positioned at a selected location beneath the floor of the reagent storage chamber 368. The stirring motor 428 includes a magnetic rotor arm 430 that spins in response to operation of the motor 428. The stirring motor 428 is located so that the bin holding the vial 374A of paramagnetic particles 422 can be positioned over the magnetic rotor arm 430 in is path toward the reagent supply station 376. In the illustrated embodiment, the stirring motor 428 is positioned in the path of the outside bins of the carrier 370 approximately 90 degrees in front of the reagent supply station 376 (measured in a clockwise direction, as Fig. 49 shows).

When the vial 374A containing the stir rod 426 stops in position over the magnetic rotor arm 430, operation of the stirring motor 428 rotates the rotor arm 430 that in turn spins the paramagnetic

stir rod 426 within the interior of the vial 374A. The spinning stir rod 426 creates a localized mixing action to resuspend the paramagnetic particles 422 generally uniformly within the suspension. The vial 374A is made of a plastic material that is not significantly effected by the spinning magnetic field created by the rotor arm 430.

Preferably, the stir rod 426 is dimensioned to occupy substantially the entire interior base area of the vial 374A to thereby maximize the effectiveness of the localized mixing action.

3. Delivery of Reagent to the Carrier

As Fig. 48 best shows, the reagent dispensing station 26 includes a reagent pipette subassembly 432 that is movable between the reagent pipetting station 354 and the reagent supply station 376 to transfer additive material from the selected reagent pack 388 (situated beneath the supply station 376) to the wells 18 of the carrier 12 (situated at the reagent pipetting station 354). The control mechanism of the reagent dispensing station 26 coordinates these fluid transfer operations, subject to the overall direction of the control module 16.

The reagent pipette subassembly 432 is in many respects similar in structure to the sample pipette subassembly 268. Like the sample pipette subassembly 268, the reagent pipette subassembly 432 includes a pair of side-by-side, stationary booms 434 and 436 that span the reagent pipetting station 354 and the reagent supply station 376. One boom 434 serves the first set of three access sites 414A/B/C in the supply station 26, while the other boom 436 serves the other set of three access sites

416A/B/C.

Also like the sample pipette subassembly 268, the reagent pipette subassembly 432 includes first and second pipettes 438 and 440, one mounted on each boom 434 and 436, respectively. Each pipette 438 and 440 also includes a probe 442 and 444 for aspirating and expelling fluid. Each probe 442 and 444 includes its own encapsulated electrical resistance heater 346 (with thermistor 348) and liquid level sensor 352, of identical construction and operation as those previously described with respect to the first probe 275 of the sample dispensing station 24 (as Fig. 47 shows). As also previously described, the heater 346 for each probe 442 and 444 maintains the desired temperature within the range of 30 and 45 degrees centigrade, to which the additive materials are heated as they are delivered to the test wells 18.

Each pipette 438 and 440 is each attached to a movable carriage (not shown) on its respective boom 434 and 436. Each carriage is independently movable upon the associated boom 434/436 in a horizontal direction (which is left and right in Fig. 48) between the associated access sites 414/416 and the reagent pipetting station 354. A carriage stepper motor 450 (shown in Fig. 4) actuated by the control mechanism, moves the associated carriage 446 horizontally on its respective boom 434/436. The carriage stepper motor 450 insures accurate movement of the probes 438 and 440 in a horizontal direction to axially align a selected probe with the desired reagent access site 414/416 and carrier well 18, subject to the overall control of the control mechanism for the reagent dispensing station 26.

The first and second pipettes 438 and 440

are also independently movable in a vertical direction (up and down) upon their respective boom by a jack screw 452 driven by a stepper motor (not shown). The jack screw stepper motor lowers and raises the associated probes 442/444 with respect to the reagent access sites 414/416 and carrier well 18, again subject to the control mechanism of the reagent dispensing station 26.

Like the previously described sample pipette subassembly 268, the reagent pipette subassembly 432 further includes a washing well 456 for each probe 442 and 444. In the illustrated embodiment (as Fig. 48 shows), the washing wells 456 are located in the path of movement of the associated probe 442/444 between the reagent pipetting station 354 and the reagent access sites 414/416.

The washing wells 456 are constructed identically to the washing well 290 shown in Figs. 43 to 46. The sequence of washing the reagent probes 442 and 444 is identical to the one previously described for the sample dispensing probes 275 and 277. The washing wells 456 associated with the reagent dispensing station 26 communicate with the washing fluid supply reservoir R6 and the waste fluid reservoir 318 (as Fig. 23 shows).

The fluid supply system 40 (see Fig. 23) includes four syringe pumps 458/460/462/464, each with an associated valve 459/461/463/465. The system 40 conveys fluid from reservoir R3 to the reagent pipette subassembly 432.

The first and second syringe pumps 458 and 460 are associated with the first reagent pipette 438, while the third and fourth syringe pumps 462

and 464 are associated with the second reagent pipette 440. The first and third pumps 458 and 462 operate during the washing cycle for their respective probes 438 and 440. The second and fourth pumps 460 and 464 serve to aspirate and dispense reagent through their respective probes 438 and 440, respectively.

The reagent syringe pumps 458/460/462/464 are constructed identical to the syringe pumps 294/296/298 associated with the sample pipette subassembly 268.

4. Sequence of Operation

In the illustrated embodiment (shown in Fig. 48), the reagent vials 374 are arranged on the reagent carrier 370 so that the outermost bin carries the vial 374A holding the paramagnetic particles 422 (with the self-contained stir rod 426); the middle bin carries the vial 374C holding the buffer solution for the sample; and the innermost bin carries the vial 374B holding the enzyme label for the particular assay.

In the illustrated embodiment, the control mechanism for the reagent dispensing station 26 fills the carrier 12 following a predetermined sequence of steps. In general, the sequence employs the first probe 442 to convey fluids to the test carrier 12 while the second probe 444 is being washed. The sequence then washes the first probe 442 while employing the second probe 444 to convey fluids to the test carrier 12.

More particularly, the sequence begins when the test carrier 12 arrives at the reagent dispensing station 26 in the manner previously described. The control mechanism actuates the

transporter 356 to bring the carrier 12 to the reagent pipetting station 354, with the first column of eight test wells, i.e., test wells (R 1 to 8, C1), into axial alignment with the path of movement of the first probe 442. In the illustrated embodiment, this column (C1) contains eight different source samples for the HBs AG assay.

During the same general period, the control mechanism actuates the carousel 406 to move the reagent pack 388 carrying the reagents for the HBs Ag assay into position under the first access site 414.

The control mechanism lifts the first probe 442 from the washing well 456. The first probe 442 then moves horizontally on the boom 434 into registration over the middle access opening 414C. The first probe 442 then lowers into the middle reagent vial 374C, and the second syringe pump 460 operates to draw reagent into the first probe 442. Meanwhile, washing fluid is being continuously conveyed by the third syringe pump 462 through the second probe 444, which is in its washing well 456.

The first probe 442 (now containing the volume of reagent) lifts from the access opening 414C. The first probe 442 then moves horizontally on the boom 434 into registration over well R1, C1. The first probe 442 then lowers into the well (R1, C1), and the second syringe pump 460 operates to expel a prescribed aliquot of the reagent into the sample contained in the well (R1, C1).

The first probe 442 then raises from the well (R1, C1) and moved one row down the first column into registration over the well (R2, C1). The probe 442 lowers, and another aliquot of the reagent is expelled. This sequence repeats for each

successive row in the first column until all eight sample wells (R1 to R8) in the column (C1) receive an aliquot of reagent.

In the illustrated embodiment, all test wells in the seventh column of the carrier 12, i.e., test wells (R1 to R8, C7), are also dedicated to the HBs Ag assay. In this arrangement, after the reagent has been added to all the wells in the first column (R1 to R8, C1), the first probe 442 raises and returns to the middle access site 414C to draw additional reagent for delivery to these test wells 18. Meanwhile, the transporter 356 operates to move the seventh column (C7) of the carrier 12 into axial alignment over the path of the first probe 442. The first probe 442 returns and moves successively down the seventh column (C7) to add the reagent to the eight additional wells (R1 to R8) dedicated to the same analytical procedure.

When the first probe 442 has completed this sequence, it moves to its washing well 456. The first syringe pump 458 operates to convey fluid to wash the first probe 442. At this time, the control mechanism also actuates the transporter 356 to position the first column of eight test wells 18, i.e., test wells (R 1 to 8, C1), into axial alignment with the path of movement of the second probe 444.

In concert with this sequence of events, while the first probe 442 is still adding reagent to the second group of test wells (R1 to R8, C7), the carousel 406 moves the reagent pack away from the reagent supply station 376 and into a position that locates the outermost vial 474A of the reagent pack over the stirring motor 428. The stirring motor 428 operates for a predetermined period (for example,

five seconds) to spin the stir rod 426 within the vial 474A to mix the paramagnetic particles 422 there contained back into the suspension. The carousel 406 then sequences to bring the reagent pack back to the reagent supply station 376, this time in registration with the second access site 416.

Upon the arrival of the reagent pack at the second access site 416, operation of the third syringe pump 462 stops, and the second probe 444 lifts from its washing well 456. The second probe 444 moves into registration over the access opening 416A of the access site 416, where the vial 474A holding the now-stirred paramagnetic particle suspension is positioned. The second probe 444 lowers, and the fourth syringe pump 464 operates to draw the suspended paramagnetic particles 422 from the vial 474A into the probe 444.

By now, the transporter 356 has moved the first column of test wells (R1 to R8, C1) into alignment with the second probe 444. The second probe 444 moves sequentially down this column (C1) adding an aliquot of the suspended paramagnetic particles 422 into each test well (R1 to R8).

The second probe 444 then returns to the access site 416A and draws another supply of suspended paramagnetic particles 422 from the vial 374A. Meanwhile, the transporter 356 operates to move the seventh column of the carrier (wells R1 to R8, C7) into axial alignment over the path of the second probe 444. The second probe 444 returns to move successively down the seventh column to add the suspended paramagnetic particles 422 to the eight additional wells (R1 to R8, C7) dedicated to the same analytical procedure.

After the second probe 444 has drawn the second batch of particles 422 to be distributed, and is conveying the particles 422 to the test wells (R1 to R8, C7), the carousel 406 operates to move another prescribed reagent pack 388 into registration with the first access site 414. This pack 388 contains the reagents and paramagnetic particles for the analytical procedure common to the samples in the second and eighth columns of the carrier 12 (which, in the illustrated embodiment is the HBc Ag assay).

When the second probe 444 has completed its task of conveying the second batch of particles 422 to the test wells (R1 to R8, C7), the second probe 444 moves to its washing well 456. The third syringe pump 462 operates to pump washing fluid through the second probe 444.

The transporter 356 moves the second column of the carrier (test wells R1 to R8, C2) into axial alignment with the path of movement for the first probe 442. The first probe 442 operates in the same fashion just described with respect to the HBs Ag assay to distribute reagent from the middle vial 374C to the eight test wells (R1 to R8) of the second and eighth columns (C2 and C8). In like fashion, the carousel 406 sequences to bring the associated vial 374A of paramagnetic particles 422 to the stirring motor 428 for mixing, and the second probe 444 operates in concert with the transporter 356 to distribute paramagnetic particles 422 to the test wells (R1 to R8) of the second and eighth columns (C2 and C8).

The sequences above described repeat for each pair of test sectors dedicated to the same assay (C1/C7; C2/C8; C3/C9; C4/C10; C5/C11; and

C6/C12). The first probe 442 distributes required reagents, while the second probe 444 washes. The second probe 444 distributes the paramagnetic particles (after mixing), while the first probe 442 washes.

After all reagents have been distributed, the control mechanism actuates the transporter 356 to return the carrier 12 to the hub access 27 for the reagent dispensing station 26 in the prescribed orientation with respect to the cutout portion 94 for pick up by the shuttle member 20. The control mechanism (which up to now has been sending back a "Busy" signal in response to periodic status inquiries from the main control module 16) now sends a "Not Busy" signal in response to the next status inquiry from the main control module 16.

Upon receipt of the "Not Busy" signal, the main control module 16 sends a command signal to the control mechanism for the shuttle member 20, instructing the control mechanism to send the shuttle member 20 to the hub access 27 to pick up the carrier 12 (to which reagents and paramagnetic particles have been added). The command signal also instructs the control mechanism for the shuttle member 20 to transport the carrier 12 to the next designated work station.

For description purposes, the remaining work stations will next be discussed in the order of the incubation station 28, the washing station 30, the substrate dispensing station 32, the reader station 34, and the carrier disposal station 36. Still, it should be recognized that the precise sequence of work stations the test carrier 12 follows after the reagent dispensing station 26 varies according to the protocols of the analytical

procedures to be performed. The precise sequence followed in the illustrated embodiment will be discussed later after the various work stations have been described.

D. The Incubation Stations

As before generally described, and as Figs. 6 to 8 show, the processing module 14 includes several individual incubation stations 28 A to I, each with its own access 29 A to I to the center hub 100. In the particular embodiment shown, there are nine incubation stations with accesses arcuately spaced and axially stacked about the center hub 100.

Each incubation station 28 A to I is constructed in the same manner, so only the incubation station 28A at the first arcuate position of the shuttle member 20 will be described in detail.

1. Delivery of the Carrier to an Incubation Station

Once the proper command signal is received from the control module 16, the shuttle member 20 transports the carrier 12 to the selected hub access 29A of the incubation station 28A. The description assumes the transport of the carrier 12 from the access for the reagent dispensing station 26 to the incubation station 28A.

In response to these commands, the shuttle member 20 rotates the platform 70 to the second arcuate position A2 to pick up the carrier 12 at the hub access 27 in the manner previously described. Once the carrier 12 is engaged, the platform 70 rotates to the first arcuate position A1. The platform 70 then moves the engaged carrier 12 into

the hub access 29A for the incubation station 28A.

The incubation station includes a support surface 92 and cutout portion 94 of the same type as previously described. It has includes a cover 93 as shown in Figs. 16 to 21.

2. Operation of the Incubation Station

The environmental control system 52 includes an electrical resistance heating element 468 located beneath the support surface of each incubation station (as Fig. 25 shows). An associated thermistor 470 maintains the heating element 468 at a desired temperature, which in the illustrated embodiment is in the range of between 30 and 45 degrees centigrade.

After a prescribed interval, the control mechanism for the incubation station 28A issues a "Not Busy" signal in response to a status inquiry from the control module 16. The control module 16 in turn issues a command signal to the shuttle member 20 to come to the incubation station 28A and pick up the carrier 12. The pick up sequence is the same as previously described with respect to the sample and reagent dispensing station 24 and 26.

The control module 16 also directs the shuttle member 20 to transport the carrier 12 to the next designated work station. For description, the next work station is assumed to be the washing station 30.

E. The Washing Station

The washing station 30 occupies a center back portion of the processing module 14 (as Fig. 4 shows).

The hub access 31 for the washing station

30 is positioned at the third arcuate position A3 of the shuttle member 20 (as Figs. 6 and 8 best show).

In the illustrated embodiment, the washing station 30 washes by dilution and aspiration. It should be appreciated, however, that the washing station 30 could wash by filtration or by other methods.

1. Delivery of the Carrier to the Washing Station

Once the proper command signal is received from the control module 16, the shuttle member 20 transports the carrier 12 to the washing station 30 access from its previous work station (which is assumed to be the incubation station access 29A) in response to additional commands issued by the shuttle control mechanism.

The washing station 30 includes a support 472 bed for receiving and transporting the carrier 12 (as Fig. 54 shows). The bed 472 has a cutout portion 94 in the hub access 31. As with the cutout portions 94 associated with the sample and reagent dispensing station 24 and 26, the shuttle platform 70 enters the washing station cutout portion 94 in its drop-off position, with the carrier 12 positioned above the plane of the bed 472. The platform 70 then lowers through the cutout portion 94 to lift the carrier 12 off the platform 70 and into the bed 472. The bed 472 includes a spaced pair of transverse grooves 96 that capture the flanged edges 86 A and B of the carrier 12 as the carrier 12 occupies the bed 472.

As Fig. 54 also shows, the washing station 30 also includes a transporter 474 that is movable axially along the bed 472 along one groove 96. The

transporter 474 is carried by a belt 476 that extends between a drive pulley 478 and an idler pulley 480. A stepper motor 482 actuated by the control mechanism for the washing station 30 rotates the drive pulley 478 and thereby advances the transporter 474 in opposite linear directions (either to the left or to the right in Fig. 54) along the bed 472.

As Fig. 56 shows, the transporter 474 includes two oppositely facing grab arms 484 and 486. Each grab arm 484 and 486 is specifically configured to capture a bottom edge of one carrier sidewall 80A or B. The transporter 474 can thereby accommodate two carriers 12 at a time, one in front (engaged by the first grab arm 484) and one behind (engaged by the second grab arm 486). The sequence of movement of the carriers 12 upon the bed 472 will be described in greater detail later.

The shuttle control mechanism acts in concert with the control mechanism for the washing station 30 to move the transporter 474 (via the stepper motor 482) into the proper positions within the hub access 31 to sequentially capture the front carrier 12 with the first grab arm 484 and then capture the rear carrier 12 with the second grab arm 486, as the shuttle platform 70 arrives and sequentially deposits the carriers 12 in the hub access 31. Subsequent actuation of the stepper motor 482 moves the carrier 12 or carriers 12 engaged by the grab arms 484 and 486 along the bed 472.

The independently operated transporter 474 frees the shuttle member 20 for other tasks while the washing process proceeds.

The washing station 30 includes a pipette

subassembly 488 to do the washing operation (see Figs. 54 and 55). The pipette subassembly 488 is arranged along a boom 490 that spans the bed 472 transversely across the path that the carrier 12 is moved by the transporter 474.

The washing station 30 is intended to perform the washing operation simultaneously upon all the samples located within an entire designated test sector (that is, R1 to R8 in each column) and, in this arrangement, sequentially upon each entire test sector in turn (that is, column by column). The transporter 474 simplifies this sequence by advancing the carrier 12 beneath the pipette subassembly 488 in stepwise fashion, one entire test sector at a time. The pipette subassembly 488 includes a series of probe sets 492 equal in number to the maximum number of test wells 18 within a given test sector defined on the carrier 12, which, in the illustrated embodiment, is eight (8). The eight (8) probe sets 492 are spaced apart a distance equal to the spacing of the wells 18 within a test sector on the carrier 12.

A stepper motor 494 actuated by the control mechanism serves to raise and lower the pipette subassembly 488 as a unit, thereby moving the probe sets 492 in unison with respect to the test sector positioned beneath them.

In the illustrated and preferred embodiment (as Figs. 57 to 59 show), each probe set 492 includes a pair of probes 496 and 498. In use, one probe 496 aspirates fluid from the associated test well 18, while the other probe 498 adds a washing liquid (typically a saline solution) to the contents of the well 18.

As Fig. 23 shows, the fluid delivery system

40 includes a pump 500 that conveys washing solution to the washing probe 498. The aspiration probe 496 communicates with the waste fluid reservoir 318 of the waste fluid system 46 via the associated vacuum pump 316 (see Figs. 23 and 24).

In the preferred arrangement (as Figs. 57 to 59 show), the aspiration probe 496 extends below the washing probe 498. The aspiration probe 496 is also offset laterally from the washing probe 498. In the preferred arrangement, the washing probe 498 generally registers with the centerline of each associated well 18, and the aspiration probe 496 is offset away from the centerline closer to a sidewall of the associated well 18. It should be appreciated that the aspiration probe 496 need not be offset from the centerline of the well 18, but could be at a range of positions closer to or along the centerline of the well 18.

In the illustrated embodiment (see Fig. 54), the bed 472 extends beyond the location of the pipette subassembly 488 a distance a sufficient distance to accommodate the two carriers 12 engaged back-to-back by the transporter 474.

The environmental control system 52 of the processing module 14 includes an electrical resistance heater 502 located under the washer bed 472 (see Fig. 55). An associated thermistor 504 maintains the heater 502 at a desired temperature, which in the illustrated embodiment is in the range of between 30 and 45 degrees centigrade.

2. General Sequence of Operation

When two carriers 12 are to be washed, the transporter 474 is first positioned with respect to the cutout portion 94 so that front grab arm 484

engages the first carrier 12 delivered to the hub access 31. The transporter 474 then advances and is repositioned by the stepper motor 482 so that the rear grab arm 486 engages the next carrier 12 delivered to the hub access 31.

Once both carriers 12 are engaged by the grab arms 484 and 486, the control mechanism operates the transporter 474 to advance the first (front) and second (rear) carrier 12 in sequence beneath the washing pipette subassembly, one test sector (i.e., one column) at a time.

When a given test column advances into position beneath the pipette subassembly 488, the transporter 474 stops, and the stepper motor 494 operates to lower the pipette subassembly 488 as a unit into each associated well 18 of the column (as Fig. 57 shows).

As Fig. 58 shows, the pipette subassembly 488 first lowers deep enough to position the longer aspiration probe 496 at a predetermined depth within the fluid adjacent the sidewall of the associated well 18. As Fig. 58 also shows, the tip 497 of the aspiration probe 496 is beveled in the direction of the sidewall and is thereby directed away from the center of each test well 18. The vacuum pump 316 of the waste fluid system 46 continuously applies a negative pressure simultaneously to all the aspiration probes 496 to draw fluid from the wells 18. The aspiration probes 496 removes a quantity of unbound materials suspended within the fluid, leaving behind within the wells 18 the solid phase supports and the complexes bound to them.

The stepper motor 494 then raises the pipette subassembly 488 so that the shorter wash probes 498 are positioned generally at the top of

each well 18 (as Fig. 59 shows). The wash pump 500 then delivers a predetermined amount of washing fluid simultaneously through each wash probe 498 into the wells 18. The washing fluid resuspends any remaining unbound material for later aspiration, as well as begins to dilute the contents of the well 18.

The transporter 474 then advances the carrier 12 the distance between adjacent columns to place the next column beneath the pipette subassembly 488. The above described aspiration/washing cycle repeats for each test column (except test columns C3 and C9 for the ALT assay, which does not undergo washing).

In the illustrated embodiment, where the complexes to be measured are bound to paramagnetic particles 422, it is desirable to concentrate the particles 422 within a preselected region of the well during the washing/aspiration process. While this result can be obtained by various methods, in the illustrated embodiment, a dynamic magnetic field (not shown) is located beneath the washer bed 472. The magnetic field varies as to direction and intensity over time to collect and concentrate the particles in the center portion of the test well. A more detailed discussion of this magnetic field appears in copending Kaul et al. U.S. Patent Application No. , entitled "Washing/Aspiration Systems and Methods for Solid Phase Assays Employing Paramagnetic Particles", which shares the same assignee as this application.

After the first and second carriers 12 are sequentially subjected to the above-described aspiration/wash cycle, the transporter 474 returns the carriers 12 back to the starting position, in

which the first column of the first (front) carrier 12 is located beneath the pipette subassembly 488. The entire aspiration/washing cycle for the first and second carriers 12 is conducted again and is thereafter repeated for a predetermined number of additional times. In the illustrated embodiment, each well 18 undergoes at least five separate aspiration/washing cycles.

After the predetermined number of aspiration/washing cycles, the transporter 474 returns the first and second carriers 12 back to the starting position, again locating the first column of the first carrier 12 in line beneath the pipette subassembly 488. The first and second carriers 12 then advance past the pipette subassembly 488 again, one column at a time, for a final aspiration cycle. In this final cycle of the washing operation, the pipette subassembly 488 lowers and raises for each column (except columns C3 and C9) only to aspirate fluid from each well 18. Unlike previous cycles, no washing fluid is added during this final cycle of the washing sequence.

It should be appreciated that the washing/aspiration sequence just described can be varied for each processing sector (carrier column). For example, different volumes of washing solution can be introduced into different processing sectors. Alternatively, one or more processing sectors can be skipped entirely, as done for columns C3 and C9 of the ALT assay. In another variation, after washing, an aspiration cycle can be skipped, thereby lengthening the separation time.

After undergoing the above-described washing sequence, the transporter 474 returns the second (rear) carrier 12 (engaged by the rear grab

arm 486) into a pick up position on the cutout portion 94 of the washer bed 472. An appropriate "Not Busy" signal is sent in response to the next status inquiry of the control module 16, which in turn issues a command signal to move the shuttle member 20 to pick up the second carrier 12 in the manner previously described. This carrier 12 is transported to the next work station according to the protocol provided.

In the illustrated embodiment, this carrier 12 is returned by the shuttle member 20 to the reagent dispensing station 26. There, the enzyme label is added to designated processing sectors on the carrier 12 in the manner previously described. The carrier 12 is then returned by the shuttle member 20 to an incubation station 28A to I in the manner previously described. After undergoing incubation for the second time, the carrier 12 is returned by the shuttle member 20 back to the washing station 30 for a second washing sequence, which is identical with the first described sequence. In this processing sequence, the carrier 12 that is to undergo a second washing sequence ultimately becomes the first (front) carrier 12 engaged by the front grab arm 484.

Immediately after the second (rear) carrier 12 has been removed from the washing station 30, and while this carrier 12 is being processed by the reagent dispensing station 26 and incubation station 28, the first (front) carrier 12 then engaged by the transporter 474 is transported to the substrate dispensing station 32 for the delivery of a substrate. In the illustrated embodiment (as Fig. 44 shows), the substrate dispensing station 32 shares the same bed 472 as the washing station 30,

and thereby shares the same hub access 31. For this reason, in the illustrated embodiment, the first (front) carrier 12 is not removed from the bed 472 after the aspiration/washing sequence, but remains there for subsequent transport directly to the substrate dispensing station 32. This sequence will be described in greater detail later.

It should be appreciated, however, that in a different arrangement, the substrate dispensing station 32 could be at a different hub access site. In this arrangement, the transporter 474 would advance the first (front) carrier 12 engaged by the front grab arm 484 to the cutout portion 94 of the bed 472 for pick up by the shuttle member 20 and transport to the substrate dispensing station 32, or whatever work station was next prescribed by the protocol.

F. <u>The Substrate Dispensing Station</u>

In the illustrated embodiment (as Fig. 54 shows), where the substrate dispensing station 32 shares the same bed 472 and hub access 31 as the washing station 30, the second (rear) carrier 12 engaged by rear grab arm 486 (which is the last carrier 12 delivered to the washing station 30) is the one that is undergoing the washing sequence for the first time, after which it is picked up by the shuttle member 20 for delivery to the reagent addition station. The first (front) carrier 12 engaged by the front grab arm 484 (which is the first carrier 12 delivered to the washing station 30) is one that is undergoing the washing sequence for the second time, after which it is to be transported directly to the substrate dispensing station 32 without further use of the shuttle member

20.

1. Delivery of the Carrier to the Substrate Station

The substrate dispensing station 32 includes a substrate pipette subassembly 506 (shown in Fig. 54) to accomplish the addition of substrate and a separate substrate aspiration subassembly 508 to accomplish the aspiration of the substrate.

The substrate pipette subassembly 506 is arranged along a boom 510 that spans the bed 472 transversely across the path of movement of the carrier 12. In the illustrated embodiment, the substrate pipette subassembly 506 is position in the path of carrier 12 movement of the bed 472 in front of the washing pipette subassembly 488, as already described. As Fig. 23 shows, the fluid delivery system 40 includes a pump 512 that conveys substrate to the pipette subassembly 506.

The substrate dispensing station 32 is intended to add substrate simultaneously to all the samples located within a designated test sector and, in this arrangement, sequentially upon each test sector in turn. The transporter 474 therefore advances the carrier 12 along the bed 472 beneath the substrate pipette subassembly 506 one entire test sector at a time. The pipette subassembly includes a series of substrate probes 514 equal in number to the maximum number of test wells 18 within a given test sector defined on the carrier 12. In the illustrated embodiment, the substrate pipette subassembly 506 therefore includes eight probes 514 spaced apart a distance equal to the spacing of the wells 18 within a test column on the carrier 12 (see Fig. 54).

A stepper motor 516 actuated by the control mechanism serves to raise and lower the substrate pipette subassembly 506 as a unit into and out of the wells 18 of the test sector positioned beneath it.

In the illustrated embodiment, the aspiration subassembly 508 for the substrate dispensing station 32 employs the same aspiration probes 496 used by the washing pipette subassembly 488. It should be appreciated, however, that different arrangements could be used. For example, the substrate pipette subassembly 506 and aspiration subassembly 508 could be positioned side-by-side or back-to-back upon the same boom 510.

2. General Sequence of Operation

After the second (rear) carrier 12 (engaged by the rear grab arm 486) has been removed by the shuttle member 20, the control mechanism operates the transporter 474 to advance the first carrier 12 beneath the substrate pipette subassembly 506, one test sector (i.e., column) at a time. When a given test column advances into position beneath the substrate pipette subassembly 506, the transporter 474 stops, and the stepper motor 516 operates to lower the pipette subassembly 506 as a unit into each associated well 18 and dispense the desired amount of substrate.

The stepper motor 516 then raises the substrate pipette subassembly 506 out of the wells 18, and the transporter 474 advances the carrier 12 the distance between adjacent columns to place the next designated column beneath the pipette subassembly 506. This sequence, as just described, repeats itself until substrate has been added to the

well 18 in all columns on the carrier 12 that are to receive substrate.

The transporter 474 then advances the carrier 12 to the aspiration subassembly 508 (which comprises the aspiration probes 496 of the washing pipette subassembly 488), positioning the first column of the carrier 12 in line beneath the subassembly 508. The aspiration-only cycle of the washing sequence repeats to draw substrate fluid from the wells 18 through the previously described aspiration probe.

Following the aspiration-only cycle of the sequence, the transporter 474 advances the carrier 12 one column at a time back through the substrate pipette subassembly 506 for the addition of another aliquot of substrate into each well 18. Preferably, in the interest of saving time, the carrier 12 moves back through in the substrate pipette subassembly 506 in an opposite direction (that is, from right to left in Fig. 54).

The above sequence of adding then aspirating wash solution (during the washing sequence), then adding and aspirating substrate, followed by the final addition of substrate (during the substrate addition cycle) in effect constitutes a buffer exchange, during which residual wash buffer is exchanged for substrate buffer.

As before explained in connection with the sequence of operation of the washing station 30, it is desirable to concentrate the paramagnetic particles 422 (when present) within the wells 18 during the substrate addition and aspiration sequences just described. the same dynamic magnetic field referred to earlier can be used for this purpose.

It should be appreciated that the substrate addition/aspiration sequence just described can be varied for each processing sector (carrier column). For example, different volumes of substrate can be introduced into different processing sectors. Alternatively, one or more processing sectors can be skipped entirely.

After the carrier 12 advances through the substrate pipette subassembly 506 for a second time, the transporter 474 returns the carrier 12 to a pick up position on the cutout portion 94 of the bed 472. A "Not Busy" signal is sent in response to the next status inquiry of the control module 16, which in turn issues a command signal to move the shuttle member 20 to pick up the carrier 12 in the manner previously described. This carrier 12 is transported to the next work station according to the protocol provided, which in the illustrated embodiment is the reader station 34.

After the first carrier 12 has passed through the substrate dispensing station 32 and has been removed by the shuttle member 20 for delivery to the reader station 34, the hub access 31 (common to the washing station 30 and substrate dispensing station 32) is open to receive two new carriers 12 in the manner described before, one for the first washing sequence and the other for the second washing sequence and subsequent addition of substrate.

G. <u>The Reader Station</u>

When viewed from the rear (as Fig. 4 shows), the reader station 34 occupies the left hand portion of the interior of the processing module 14. The hub access 35 for the reader station 34 is

positioned at the fourth arcuate position A4 of the shuttle member 20, being arcuately spaced about one hundred and eighty degrees from the hub accesses 27 and 29D/E/F, and about ninety degrees from the hub accesses 31 and 29 G/H/I (in a clockwise direction) and 23, 25, and 29A/B/C (in a counterclockwise direction) (see Fig. 8). The hub access 35 for the reader station 34 is generally in the same horizontal plane as the hub accesses 23 and 27 (for the carrier dispensing station 22 and the reagent dispensing station 26, respectively) (see Fig. 6).

1. The Optical Subassembly

The reader station 34 (as Fig. 60 shows) includes an optical subassembly 518 for measuring the fluorescence of the samples contained in the carrier 12.

The optical subassembly 518 includes an excitation tube 520 that communicates with a xenon light source 522 on one end and a photomultiplier tube 524 on the other end that itself communicates with a fluorescence sensor 526. A filter block 528 is located between the excitation tube 520 and the photomultiplier tube 524. The filter block 528 includes a dichroic lens 530 that directs incoming light from the excitation tube 520 to the sample and directs the outgoing fluoresced light from the sample through the photomultiplier tube 524 to the sensor 526.

The filter block 528 (see Fig. 61 also) includes one or more emission filters 532 that are selectively moveable into the light path extending between the excitation tube 520, the sample and the photomultiplier tube 524. Each emission filter 532 selects out a desired wave length of fluoresced

light that is to be measured by the sensor 526, which wave length depends upon the particular assay being read.

As Fig. 61 shows, the filter block 528 is attached to a carrier 534 that is connected via a drive belt 536 and pulley 538 to a stepper motor 540. The control mechanism for the reader station 34 operates the stepper motor 540 to move the desired emission filter 532 into registration with the light path between excitation tube 520 and photomultiplier tube 524.

As Fig. 60 shows, a silicon detector 542 is provided to sense the presence of incoming light in the excitation tube 520. A lens 544 is provided in the filter block 528 in association with each emission filter 532 to pass incoming light through the dichroic lens 530 to the silicon detector 542. The absence of incoming light by the detector 542 (should the light source 522 fail) generates an error signal.

2. **Deliver of the Carrier to the Reader Station**

Once the proper command signal is received from the control module 16, the shuttle member 20 transports the carrier 12 to the hub access 35 from its previous work station (which is assumed to be the substrate dispensing station 32) in response to additional commands issued by the shuttle control mechanism.

As Figs. 60 and 62 show, the reader station 34 includes a bed 546 positioned beneath the optical subassembly 518 for receiving the carrier 12. The bed 546 has the same type of cutout portion 94 as the other work stations, situated at the hub access

35. As before described, the shuttle platform 70 enters this cutout portion 94 with the carrier 12 and then lowers through the cutout portion 94 to lift the carrier 12 off the platform 70 and into the bed 546.

As Fig. 60 also shows, the bed 546 also includes the spaced pair of transverse grooves 96 that capture the flanged edges 86A/B of the carrier 12 as the carrier 12 is placed onto the bed 546. The bed 546 also includes a keyway 548 that engages the notched keyway 82B formed on the carrier sidewall 78B, thereby holding the carrier 12 in position on the bed 546.

As Fig. 62 shows, the environmental control system 52 includes electrical resistance heaters 550 located in a dropped ceiling 551 above the bed 546. Associated thermistors (not shown) maintain the heaters 550 at a desired temperature (which is in the range of between 30 and 45 degrees centigrade in the illustrated embodiment).

3. Positioning the Carrier With Respect to the Optical Subassembly

The reader station 34 includes a transport mechanism 554 (best shown in Fig. 62) that moves the bed 546 to selectively position the carrier 12 with respect to the optical subassembly 518. This frees the shuttle member 20 to perform other functions during the reading process.

Using the transport mechanism 554, each test well 18 can be individually positioned beneath the optical subassembly 518 on a selective basis.

The transport mechanism 554 includes a first transporter 556 that moves the bed 546 in a first path (shown by arrows in Fig. 62) that is

generally parallel to the direction that the rows are laid out on the carrier 12 (which is from left to right when viewed from the access 35 in Fig. 62).

The transport mechanism 554 also includes a second transporter 558, operable independent of the first transporter 556, that moves the bed 546 in a second path (shown by arrows in Fig. 62) that is generally parallel to the direction that the columns are laid out on the carrier 12 (which is fore and aft when viewed from the access 35 in Fig. 62).

The transport mechanism 554 can be variously constructed. In the illustrated embodiment, the first transporter 556 includes a support base 560 upon which the bed 546 is movable in the first path. One side of the bed 546 slidably engages a guide bar 562 on the support base 560, while the other side of the bed 546 includes guide wheels 564 that travel within a trackway on the support base 560. A belt drive 566 coupled to a stepper motor 568 moves the bed 546 in the first path upon the support base 560.

The support base 560 itself is supported for movement upon another pair of guide bars 570. Another drive belt 572 coupled to another stepper motor 574 moves the support base 560 in the second direction along the guide bars 570.

4. Sequence of Operation

After the carrier 12 has been delivered to the reader bed 546, the stepper motors 568 and 574 are independently operated actuated by the reader station control mechanism to position the individual test wells 18 with respect to the optical subassembly 518. The stepper motor 540 also operates to position the desired emission filter 532

in the light path. The optical subassembly 518 then operates to take the desired reading.

In the illustrated embodiment, the optical subassembly 518 takes sequential readings of the test wells 18 within a given sector (arranged by column) by proceeding sequentially test well by test well (row by row) through the sector.

In this sequence, the bed 546 is first positioned to bring the first test well 18 of the desired test sector (column) into operative alignment with the optical subassembly 518. The optical subassembly 518 operates to take the first kinetic reading for that test well 18, which is the measured fluorescence of that sample. The stepper motor 574 of the second transporter 558 operates to move the bed 546 to bring the next test well 18 of the desired sector into operative alignment with the optical scanner, and the first kinetic reading for that test well 18 is taken. The sequence repeats until all the test wells 18 of the column advance past the optical subassembly 518, and all the first kinetic readings are taken.

The transport mechanism 554 then operates to bring the test wells 18 for the next designated test sector into successive operative alignment with the optical subassembly 518 for another series of first kinetic readings. The first kinetic readings for the test wells are individually stored in the mass storage device 134 of the control module 16.

Once all the desired first kinetic readings are taken for the specimens contained on the carrier 12, the bed 546 returns to the pick up position for the shuttle member 20. A "Not Busy" signal is sent to the control module 16. The control module 16 in turn issues a command signal to move the shuttle

member 20 to pick up the carrier 12 at the hub 100 access in the manner previously described. The carrier 12 is transported to an available one of the incubation stations 28 A to I for a prescribed period, after which time it is returned back to the reader station 34 for a second series of kinetic readings. The second series of kinetic readings is also stored in the mass storage device 134 of the control module 16.

The results of the first kinetic reading and the second kinetic reading are compared for each well 18 to figure out the change in measured fluorescence over time. This change in measured fluorescence over time represents the ultimate quantitative measurement obtained for that particular assay for that particular sample. The results are transmitted to the control module 16 for display in a user reader format via the printer.

Simultaneously, the shuttle member 20 is sent to transport the carrier 12 to the next work station according to the protocol provided. In the illustrated arrangement, the next station is the carrier disposal station 36.

H. <u>The Carrier Disposal Station</u>

The carrier disposal station 36 shares the same hub access 35 as the reader station 34 (as Fig. 62 shows).

The carrier disposal station 36 includes a bed 576 having a cutout portion 94 situated at the hub access 35 (as Fig. 63 also). As before described, the shuttle platform 70 enters this cutout portion 94 with the carrier 12 and then lowers through the cutout portion 94 to lift the carrier 12 off the platform 70 and into the bed 576.

The bed 576 also includes a spaced pair of transverse grooves 96 that capture the flanged edges 86A/B of the carrier 12 as the carrier 12 is placed onto the bed 576.

As Figs. 64 and 65 show, the bed 576 rests upon a trap door 577 over an exit opening 578. The exit opening 578 leads to a chute 580 that leads to a carrier waste container 582, which occupies the same compartment 50 as the waste fluid container 50 (see Fig. 1).

The trap door 577 is attached by a shaft 586 to a stepper motor 588. The stepper motor 588 normally retains the trap door 577 and the bed 576 in a generally horizontal position (shown in Figs. 63 and 64). Upon receipt of a signal from the control mechanism for the carrier disposal station 36, the stepper motor 588 rotates the shaft 586 to tip the trap door 577 and the bed 576 (as Fig. 65 shows). The stepper motor 588 then operates to return the trap door 577 and the bed 576 back to the horizontal position.

The bed 576 is retained in its horizontal position to receive the carrier 12 from the shuttle member 20 through the hub access 35. After the shuttle member 20 is withdrawn from the hub access 35, the stepper motor 588 operates to tip the bed 576. The carrier 12 slides off the bed 576 through the exit opening 578 and chute 580 and into the waste container 582 (as Fig. 65 shows). The bed 576 is returned to its horizontal position to await the receipt of another carrier 12 for disposal.

III. FURTHER SPECIFIC DESCRIPTION OF CONTROL MODULE IN THE PREFERRED EMBODIMENTS

Fig. 66 diagrammatically shows the time

sequence of the protocols to the HBs Ag assay; the HBc Ag assay; the HIV-1 Ab assay; HTLV-I Ab assay; and the TPA Ab assay. Fig. 67 diagrammatically shows the time sequence of the protocol for the ALT assay.

In the illustrated embodiment, the master control schedule 590 consolidates the various requirements of the individual protocols performed on a single carrier 12 in terms of step sequence, step timing, and other operating parameters for each carrier 12. The master control schedule 590 also introduces additional carriers 12 for processing in the system 10 at prescribed time intervals, and after that coordinates the performance of the individual protocols for each carrier 12 present in the system 10 at a given time.

The master control schedule 590 thereby establishes a consolidated timing sequence by which all the different immunoassays procedures are to be performed on the multiple test carriers 12 present in the processing module 14. In a preferred sequence, the master control schedule introduces a new test carrier 12 into the system 10 about every eight minutes. Each test carrier 12 remains in the system 10 about 120 minutes, during which time the six different immunoassay procedures are performed on the sixteen source specimens contained on the carrier 12, following the time sequences shown in Figs. 66 and 67.

In this way, the master control schedule coordinates the independent operation of the shuttle member 20 and the eight processing stations to carry out approximately 120 immunoassays per hour.

In the illustrated and preferred embodiment, the CPU 122 of the control module 16

also creates a status report continuously displayed on the video monitor 130 to show the user the position of each test carrier 12 within the processing system 10 at a given time.

IV. CONCLUSION

The description of the analytical system 10 in the illustrated embodiments is not intended to limit the scope of the invention to the particular types of assay or particular assay techniques involved. The analytical system 10 that embodies the invention can employ different assay procedures and different assay techniques, ones that do not rely upon immunochemical reactions, or use a solid support to bind the complexes, or rely upon fluorescent substrates. It will be seen and appreciated that the invention is applicable for use with diverse analytical types and techniques, though they are not all described in detail in this application.

The features and advantages of the various aspects of the invention are set forth in the claims that follow.

CLAIMS

We claim:

1. A system for conducting an analytical procedure comprising:

a test carrier comprising means for retaining at least one sample to be analyzed,

a work station having an access for receiving the test carrier and processing means for performing at least one processing task on the sample retained on the test carrier,

shuttle means for delivering the test carrier to and from the processing station access, and

transport means on the work station movable independently of the shuttle means and operative for moving the test carrier within work station.

2. A system according to claim 1

wherein the access for the work station is spaced from the processing means, and

wherein the transport means is operative for moving the test carrier between the access and the associated processing station within the work station.

3. A system according to claim 1

and further including a second work station having an access spaced from the access for the first defined work station and including processing means for a task associated with the procedure,

and wherein the shuttle means is operative for delivering a second test carrier to and from the access of the second work station while the transport means independently operates to move the first delivered test carrier within the first work station.

4. A system according to claim 3

wherein the second work station includes second transport means operable independent of the shuttle means and the first defined transport means for moving the second test carrier within the second work station while the first transport means operates independently to move the first test carrier within the first work station.

5. A system according to claim 1

wherein the test carrier includes a first and second designated processing sectors and means for retaining at least one sample to be analyzed within the first designated sector and for retaining at least one other sample to be analyzed within the second designated sector, and

wherein at least one of the work stations includes means for performing a first specified processing task on the sample retained in the first designated sector and for performing a second specified processing task on the sample retained in the second designated sector.

6. A system according to claim 1

wherein the transport means is operative for moving two test carriers within the work station.

7. A system according to claim 1

wherein the transport means is operative for moving the carrier in at least two different directions within the work station.

8. A system according to claim 1

wherein the work station includes a support surface for the carrier, and

wherein the transport means is operative for moving the support surface, thereby moving the carrier.

9. A system according to claim 1

wherein the work station includes a support surface for the carrier, and

wherein the transport means is movable along the support surface and includes means for releasably engaging the carrier for movement.

10. A system according to claim 1 and further including

container means for storing a component used by the processing means in performing its processing task, and

second transport means operable independently of the first mentioned transport means and the shuttle means for delivering the container means to the processing station.

11. A system according to claim 10

wherein the processing station dispenses samples to be analyzed to the carrier, and

wherein the container means stores a quantity of a source specimen for dispensing by the processing means.

12. A system according to claim 10

wherein the processing station dispenses reagent materials to the carrier, and

wherein the container means stores a quantity of a source reagent for dispensing by the processing means.

13. A system for conducting an analytical procedure comprising:

a test carrier comprising a first region for retaining a fluid to be analyzed and a second region, spaced from the first region, for retaining a fluid to be analyzed,

a work station having an access for receiving the test carrier and processing means including at least one pipetting means for

dispensing aliquots of fluid,

shuttle means for delivering the test carrier to and from the processing station access, and

transport means on the work station operable independently of the shuttle means for moving the test carrier within work station to align a selected one of the regions with the pipetting means for dispensing the fluid thereto.

14. A system according to claim 13 and further including

container means for storing a fluid to be dispensed,

second transport means operable independently of the first mentioned transport means and the shuttle member for delivering the container means to the pipetting means for conducting fluid from the container means into the pipetting means.

15. A system according to claim 14

wherein the pipetting means conducts fluid from the container means at a first work area within the station and dispenses the conducted fluid to the carrier at a second work area within the station,

and further including third transport means for moving the pipetting means between the first and second work areas independent of the first and second transport means and the shuttle means.

16. A system according to claim 15

wherein the work station includes means for washing the pipetting means at another work area spaced from the first and second work areas, and

wherein the third transport means is operative for moving the pipetting means among the first, second, and other work areas independent of the first and second transport means and the shuttle

means.

17. A system according to claim 13

wherein the work station includes second pipetting means operable independent of the first mentioned pipetting means for dispensing fluid, and

wherein the transport means is operative for moving the test carrier within work station to align a selected one of the regions with a selected one of the pipetting means for dispensing the fluid thereto.

18. A system according to claim 17

and further including container means for storing a fluid to be dispensed, and

second transport means operable independently of the first mentioned transport means and the shuttle member for delivering the container means to a selected one of the pipetting means for conducting fluid from the container means into the selected pipetting means.

19. A system according to claim 18

wherein the first mentioned pipetting means conducts fluid from the container means at a first work area within the station and dispenses the conducted fluid to the carrier at a second work area within the station,

wherein the second pipetting means conducts fluid from the container means at a third work area within the station and dispenses the conducted fluid to the carrier at a fourth work area within the station,

and further including third transport means for moving the first pipetting means between the first and second work areas and fourth transport means for moving the second pipetting means between the third and fourth work areas, the third and

fourth transport means operating independently of the first and second transport means and the shuttle means.

20. A system according to claim 19

wherein the work station includes means for washing the first pipetting means at a fifth work area and for washing the second pipetting means at a sixth work area spaced from the fifth work area, the fifth and sixth work area also being spaced from the first through fourth work areas,

wherein the third transport means is operative for moving the first pipetting means among the first, second, and fifth work areas and the fourth transport means is operative for moving the second pipetting means among the third, fourth, and sixth work areas independently of the first and second transport means and the shuttle means.

21. A system according to claim 20

wherein, while the third transport means operates to move the first pipetting means between the first and second work areas to conduct and dispense fluid, the fourth transport means operative to maintain the second pipetting means in the sixth work area for washing.

22. A system according to claim 20 or 21

wherein, while the fourth transport means operates to move the second pipetting means between the third and fourth work areas to conduct and dispense fluid, the third transport means operative to maintain the first pipetting means in the fifth work area for washing.

23. A system for conducting an analytical procedure comprising:

a test carrier comprising means for retaining at least one sample to be analyzed,

a work station having an access for receiving the test carrier and processing means for performing at least one processing task on the sample retained on the test carrier,

shuttle means for delivering the test carrier to and from the processing station access,

transport means on the work station operable independently of the shuttle means in a first mode for receiving the test carrier at the work station access, a second mode for moving the test carrier for processing at the processing means, and a third mode for returning the carrier to the work station access, and

control means for periodically sensing the mode of operation of the transport means and for generating a signal to operate the shuttle means in response to the mode of operation sensed.

24. A system according to claim 23

wherein the control means is operative, when sensing the transport means is in its first mode of operation, for operating the shuttle means to deliver a carrier to the work station access; when sensing the transport means is in its third mode of operation, for operating the shuttle means to pick up a carrier at the work station access; and when sensing the transport means is in its second mode of operation, for operating the shuttle means in areas outside the work station access.

25. A system for conducting an analytical procedure comprising:

a test carrier comprising means for retaining at least one sample to be analyzed,

a first work station for storing at least one test carrier and including an access and means for dispensing the stored test carrier to the access

upon receipt of a command signal,

a second work station having an access for receiving the test carrier and processing means for performing at least one processing task on the sample retained on the test carrier,

shuttle means for receiving, transporting, and delivering a test carrier in response to command signals,

transport means on the second work station moveable independently of the shuttle means and operable in response to command signals in a first mode for receiving the test carrier at the work station access, a second mode for moving the test carrier for processing at the processing means, and a third mode for returning the carrier to the work station access,

master control means for coordinating the operation of the transport means and shuttle means including means for periodically sensing the mode of operation of the transport means and for generating command signals in response to the mode of operation sensed, the control means being operative, when sensing the transport means is in its first mode of operation, for generating command signals to dispense a test carrier at the first access and to operate the shuttle means to pick up the dispensed test carrier at the first access and deliver the dispensed carrier to the second access; when sensing the transport means is in its third mode of operation, for generating command signals to operate the shuttle means to pick up a carrier at the second access; and when sensing the transport means is in its second mode of operation, for generating command signals to operate the shuttle means in areas outside the second access.

26. A system according to claim 25

and further including a third work station having an access for receiving the test carrier and processing means for performing at least one processing task on the sample retained on the test carrier, and

wherein the control means is operative, when sensing the transport means is in its third mode of operation, for generating command signals to operate the shuttle means to pick up a carrier at the second access and deliver the carrier at the third access.

27. A system according to claim 26

and further second transport means on the third work station moveable independently of the shuttle means and the first mentioned transport means, the second transport means being operable in response to command signals for moving the test carrier for processing at the associated processing means, and

wherein the master control means coordinates the operation of the second transport means with the first transport means and the shuttle means.

28. A system according to claim 27

wherein the second transport means is operable in a first mode for receiving the test carrier at the third access, a second mode for moving the test carrier for processing at the associated processing means, and a third mode for returning the carrier to the third access, and

wherein the master control means includes means for periodically sensing the mode of operation of both the first and second transport means and for generating command signals in response to the modes

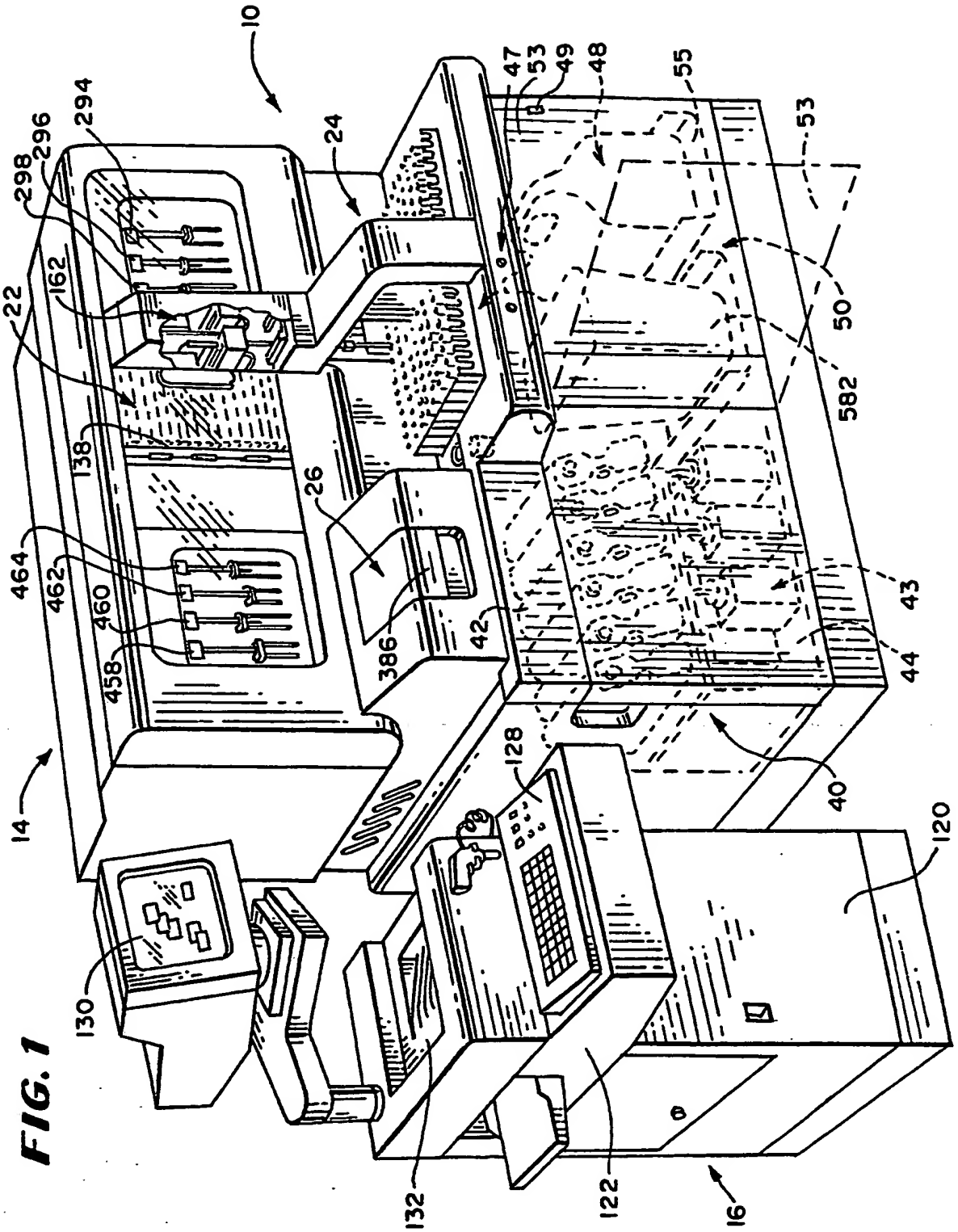
of operation sensed, the control means being operative, when sensing the first transport means is in its third mode of operation, for generating command signals to operate the shuttle means to pick up a carrier at the second access and for delivering the carrier to the third access only if sensing that the second transport means is also in its first mode of operation.

29. A system according to claim 28

wherein the master control means is operative, when sensing the second transport means is in its second mode of operation, for generating command signals to operate the shuttle means in areas outside the third access.

30. A system according to claim 28

wherein the master control means is operative, when sensing the second transport means is in its third mode of operation, for generating command signals to operate the shuttle means to pick up a carrier at the third access; and when sensing the second transport means is in its second mode of operation, for generating command signals to operate the shuttle means in areas outside the third access.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48
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298
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582
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16

FIG. 1

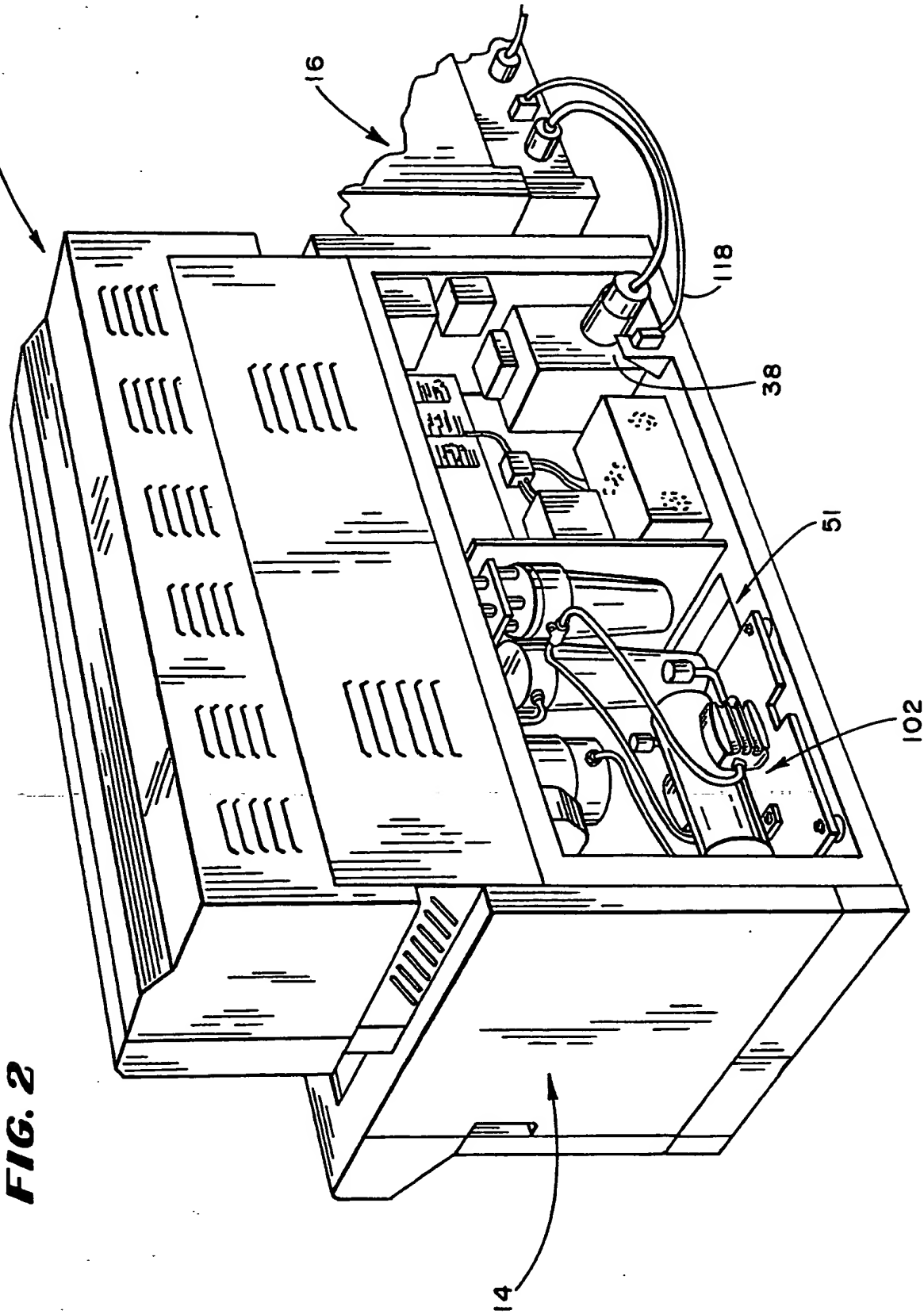
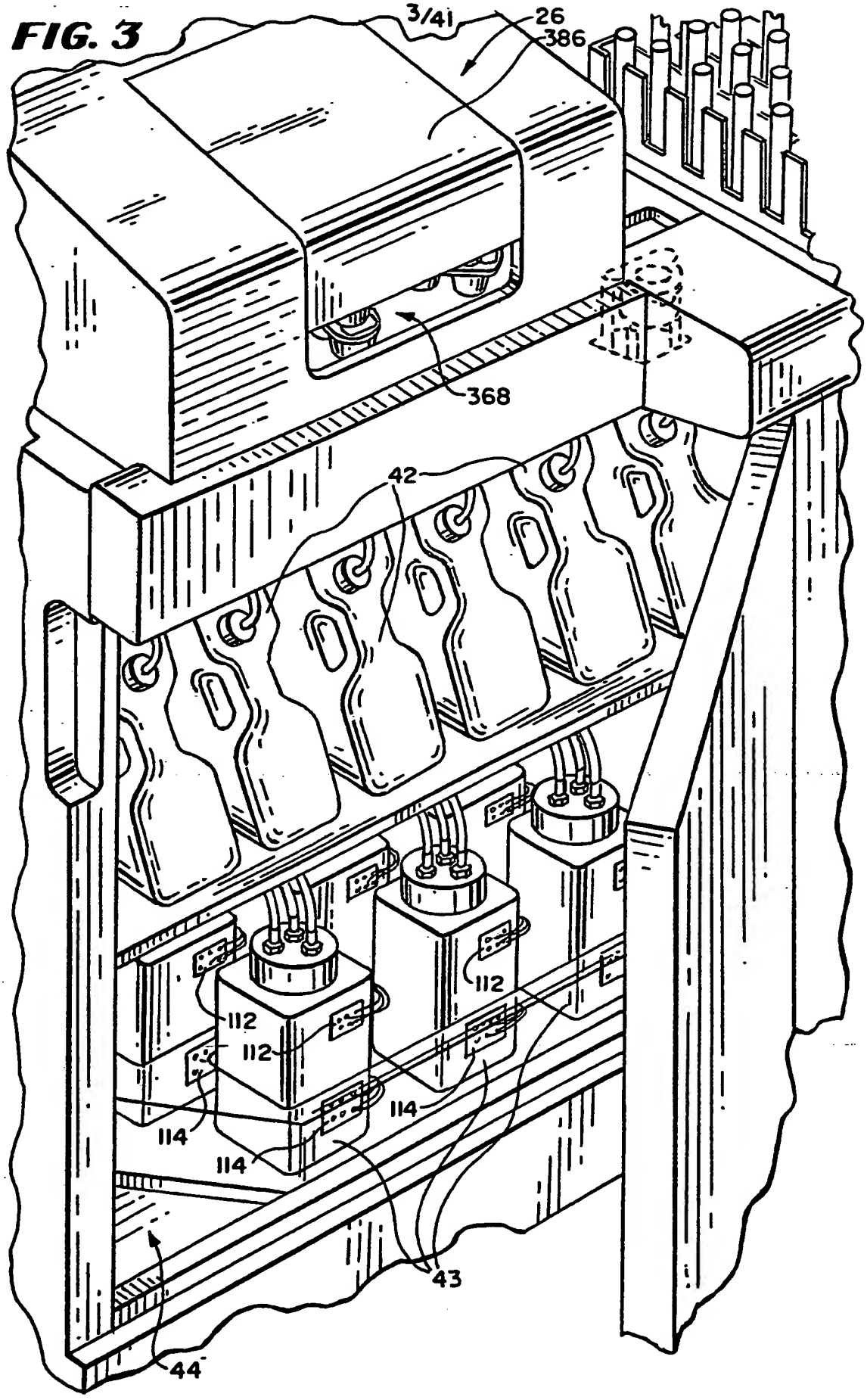


FIG. 2

FIG. 3



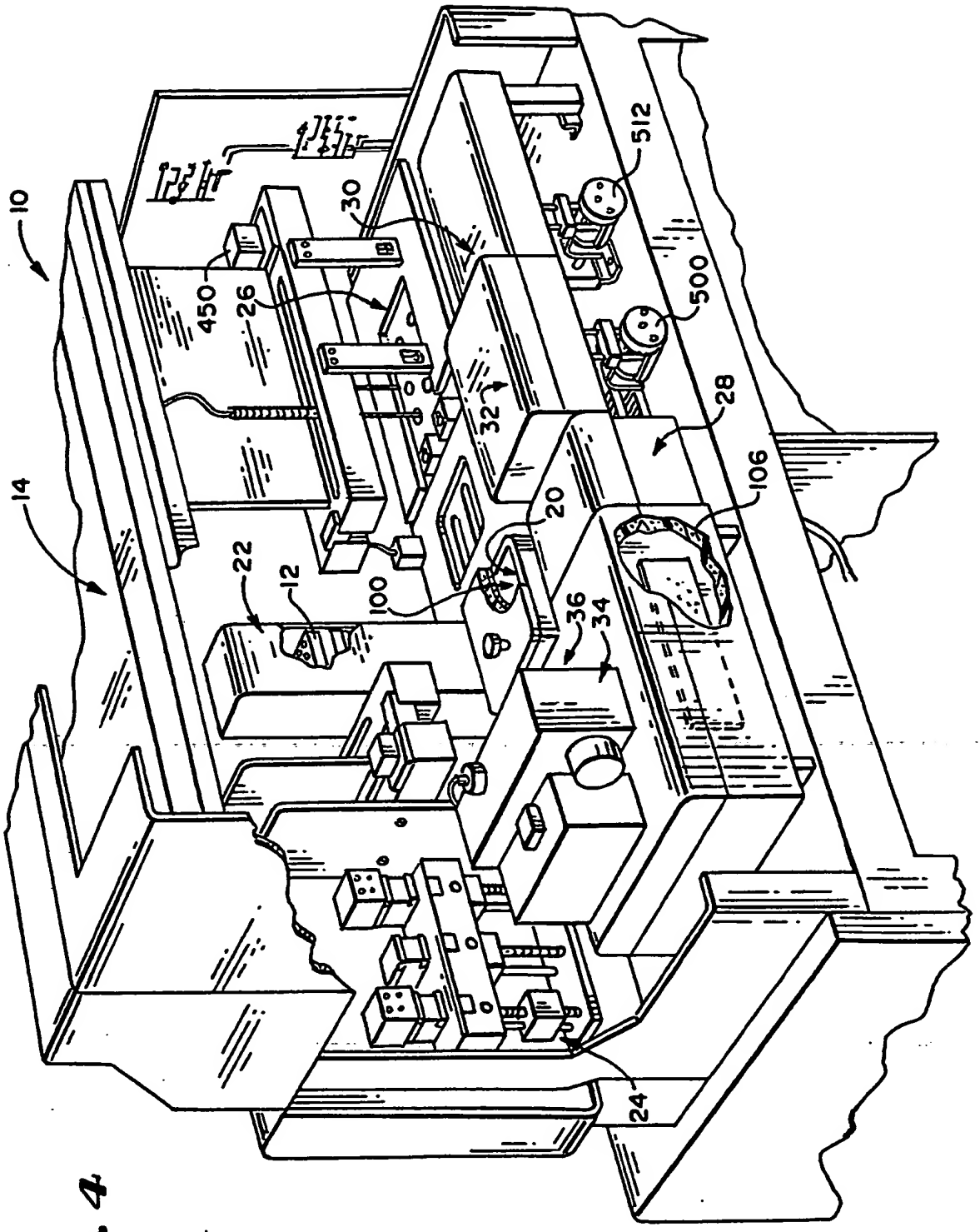


FIG. 4

FIG. 5

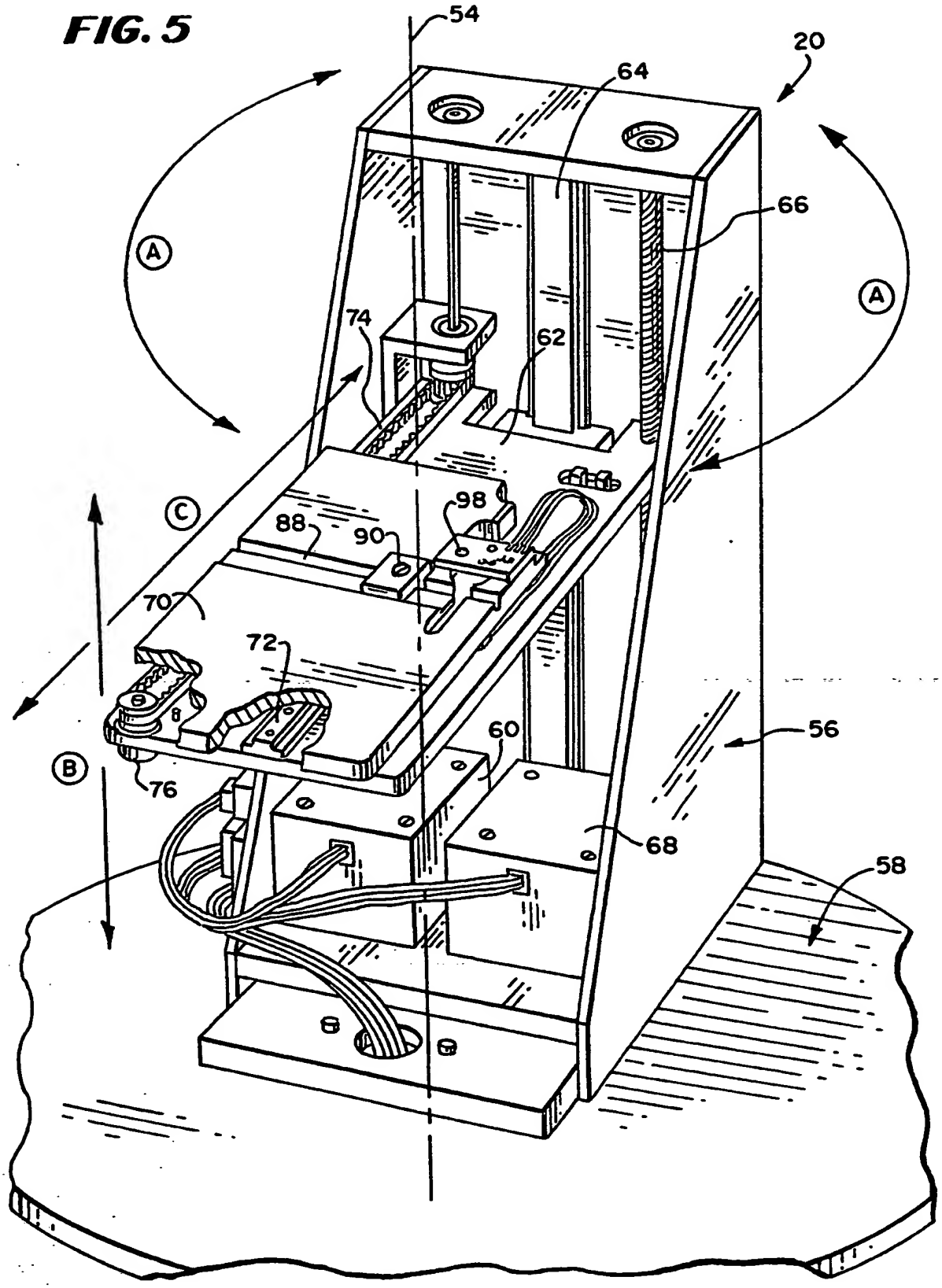


FIG. 6

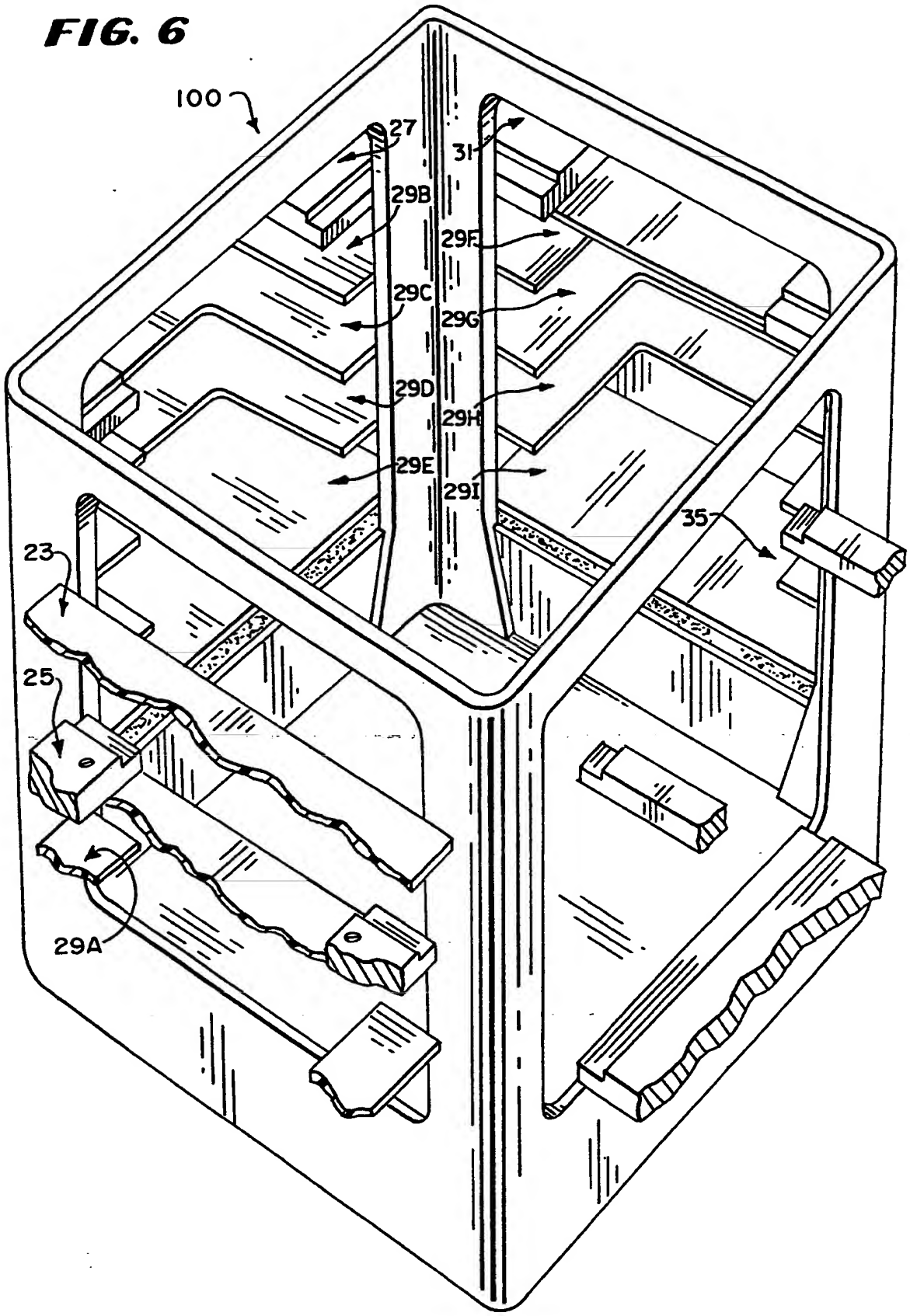
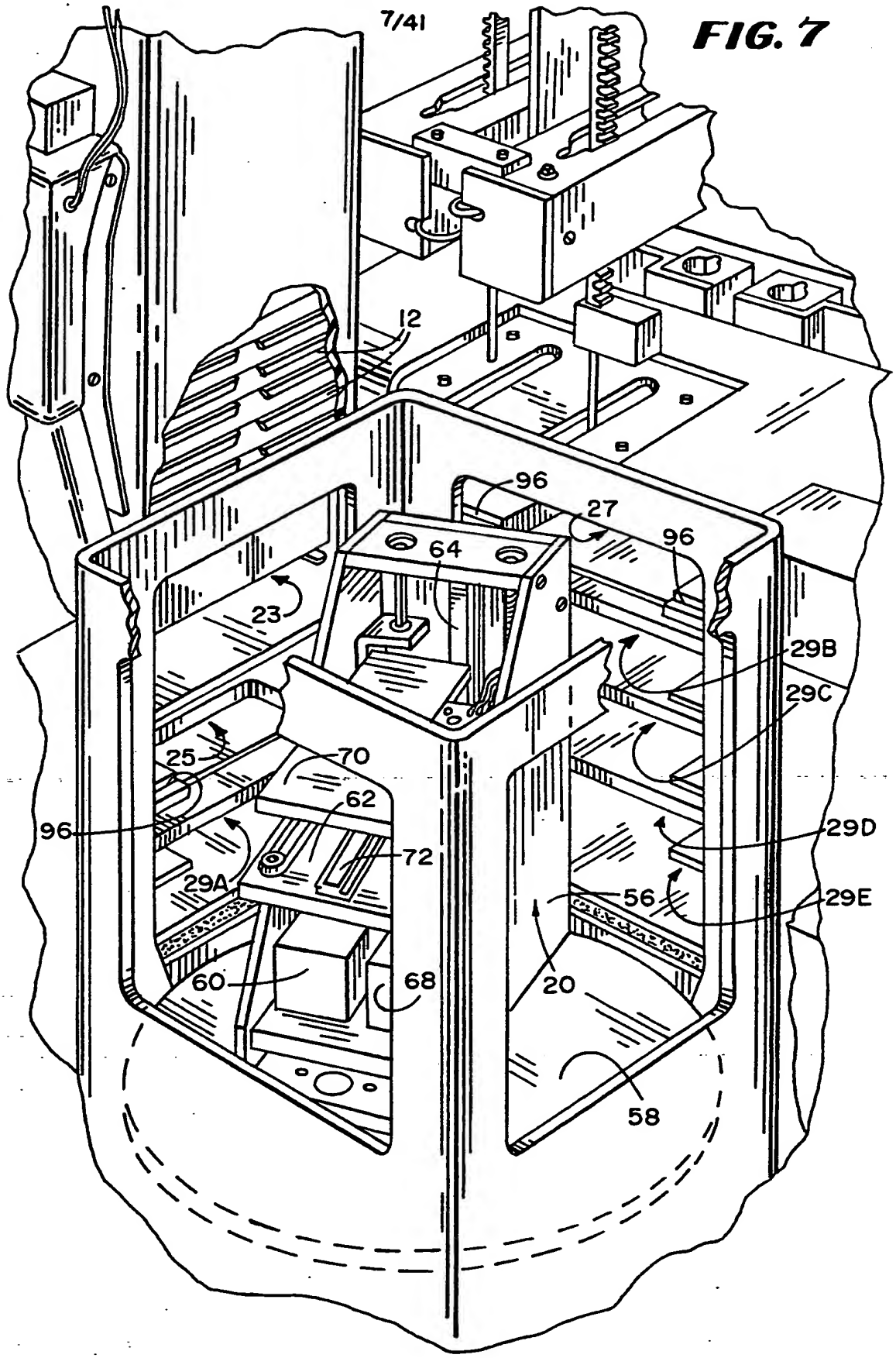


FIG. 7



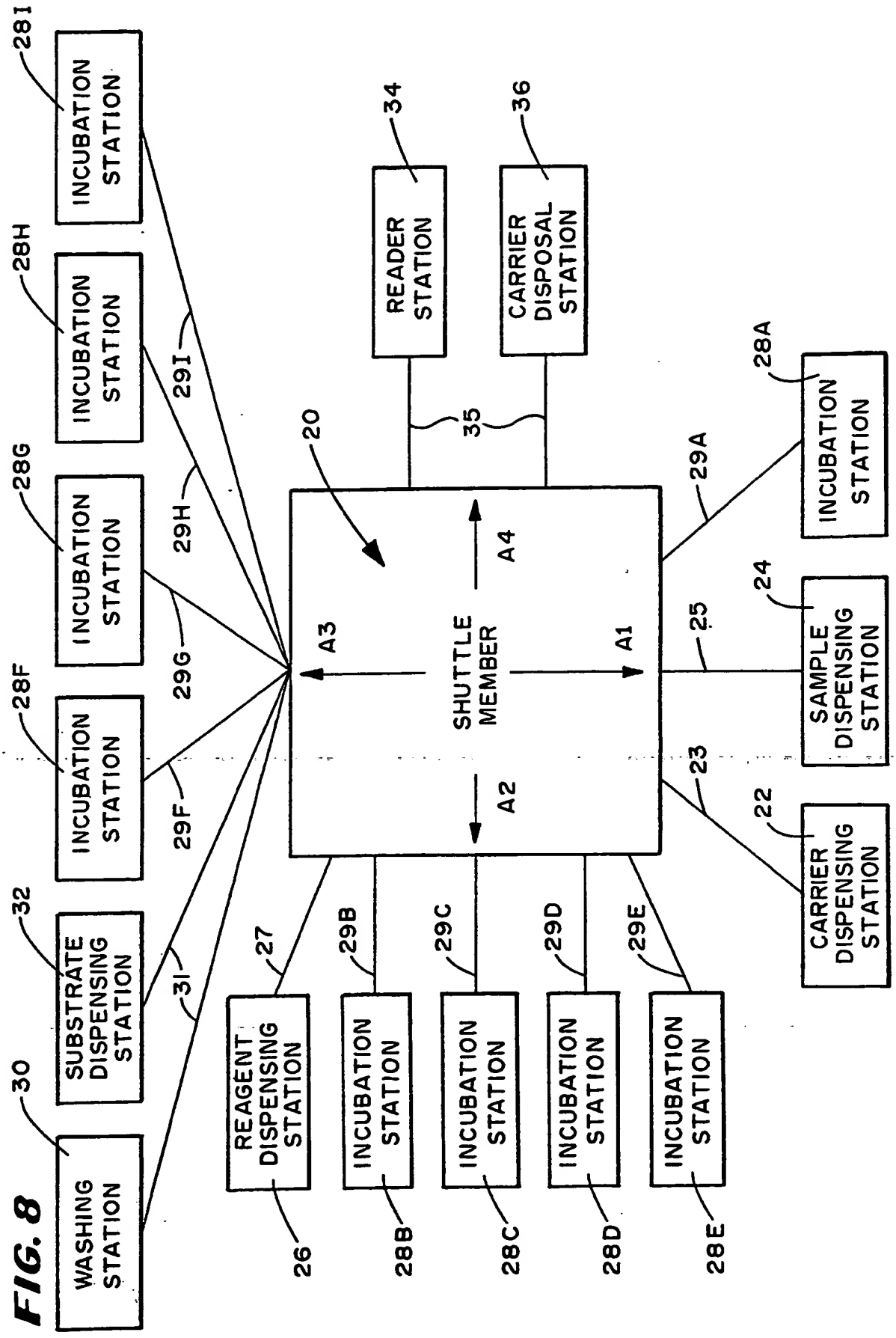

WASHING STATION
30
SUBSTRATE DISPENSING STATION
32
INCUBATION STATION
28F
INCUBATION STATION
28G
INCUBATION STATION
28H
INCUBATION STATION
28I
REAGENT DISPENSING STATION
26
INCUBATION STATION
28B
INCUBATION STATION
28C
INCUBATION STATION
28D
INCUBATION STATION
28E
CARRIER DISPENSING STATION
22
SAMPLE DISPENSING STATION
24
INCUBATION STATION
28A
READER STATION
34
CARRIER DISPOSAL STATION
36
SHUTTLE MEMBER
20
A1
A2
A3
A4
31
29F
29G
29H
29I
27
29B
29C
29D
29E
23
25
29A
35

FIG. 8

FIG. 9

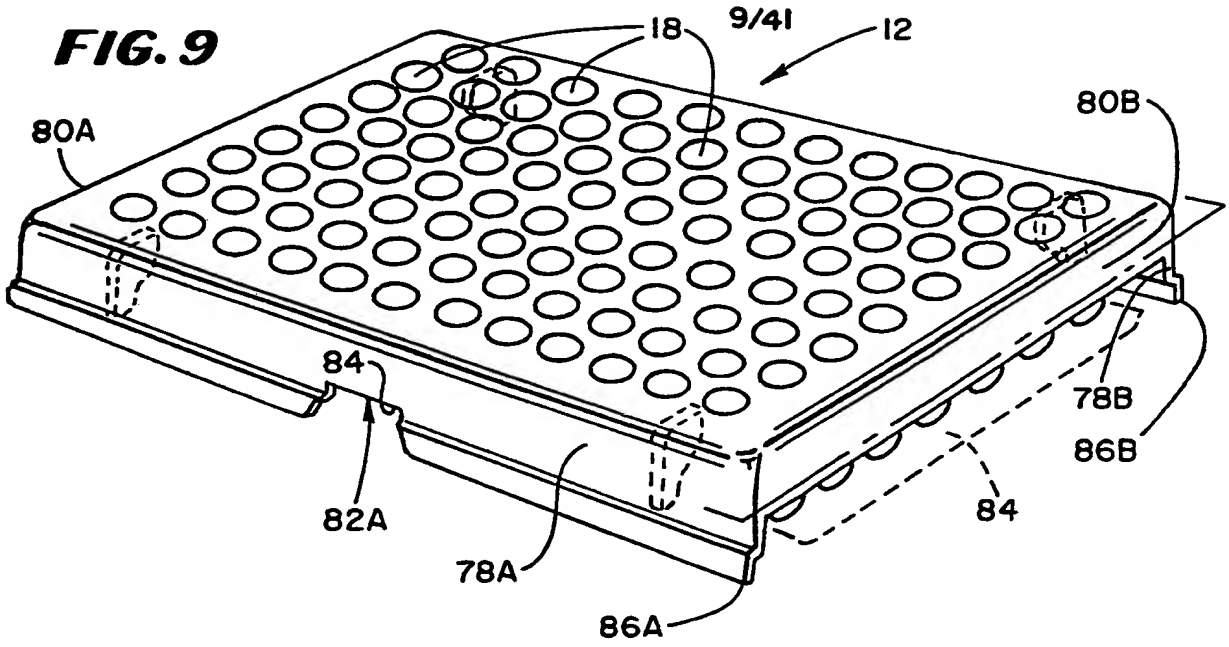

18
9/41
12
80B
80A
84
78B
86B
82A
84
78A
86A

FIG. 10

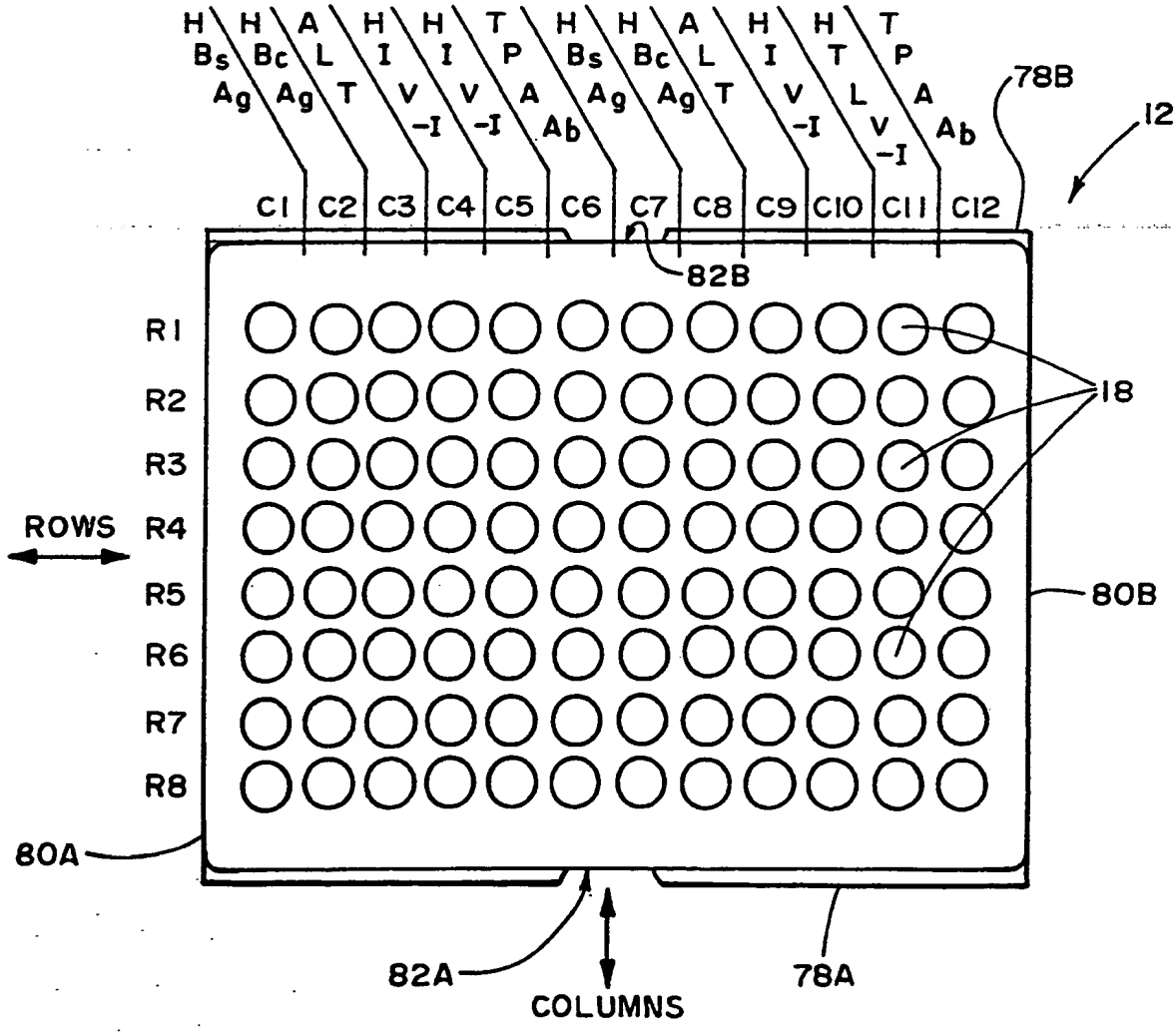
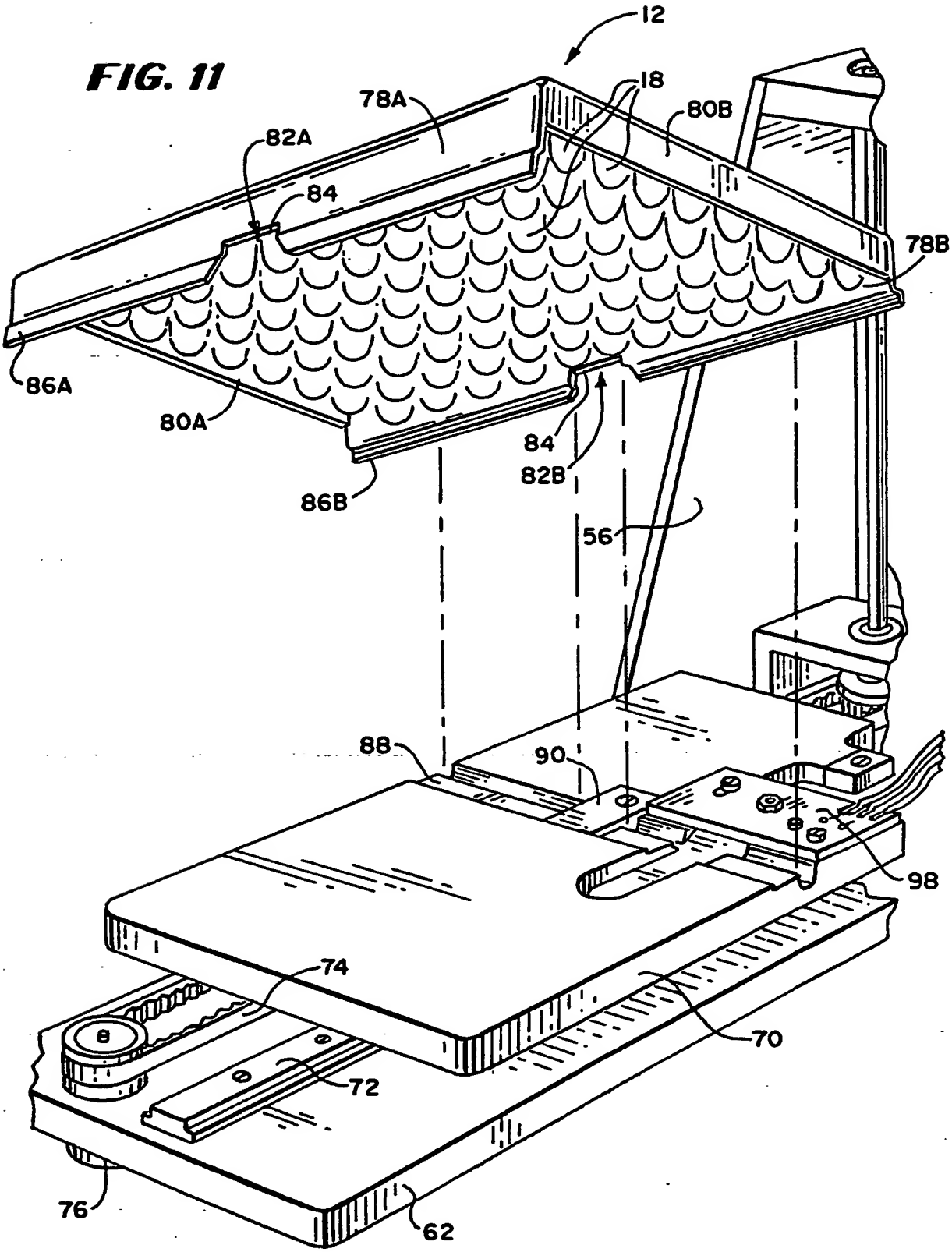

HBsAg
HBcAg
ALT
HIV-I
HIV-I
TPAAb
HBsAg
HBcAg
ALT
HIV-I
HTLV-I
TPAAb
78B
12
C1 C2 C3 C4 C5 C6 C7 C8 C9 C10 C11 C12
82B
R1
R2
R3
R4
R5
R6
R7
R8
ROWS
18
80B
80A
82A
78A
COLUMNS

FIG. 11


12
18
78A
80B
82A
84
78B
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80A
84
82B
86B
56
88
90
98
74
70
72
76
62

FIG. 12

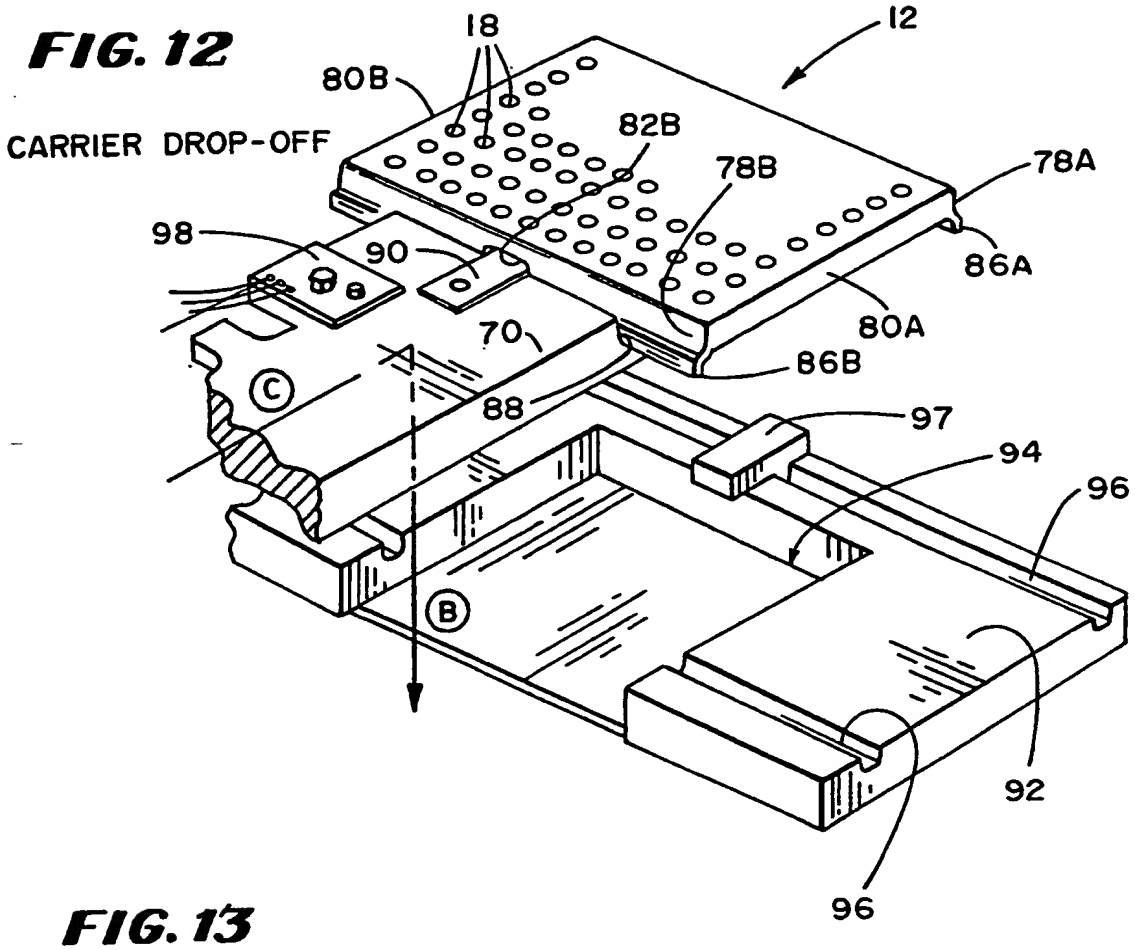

CARRIER DROP-OFF
18
12
80B
82B
78B
78A
98
90
86A
80A
70
86B
C
88
97
94
96
B
92
96

FIG. 13

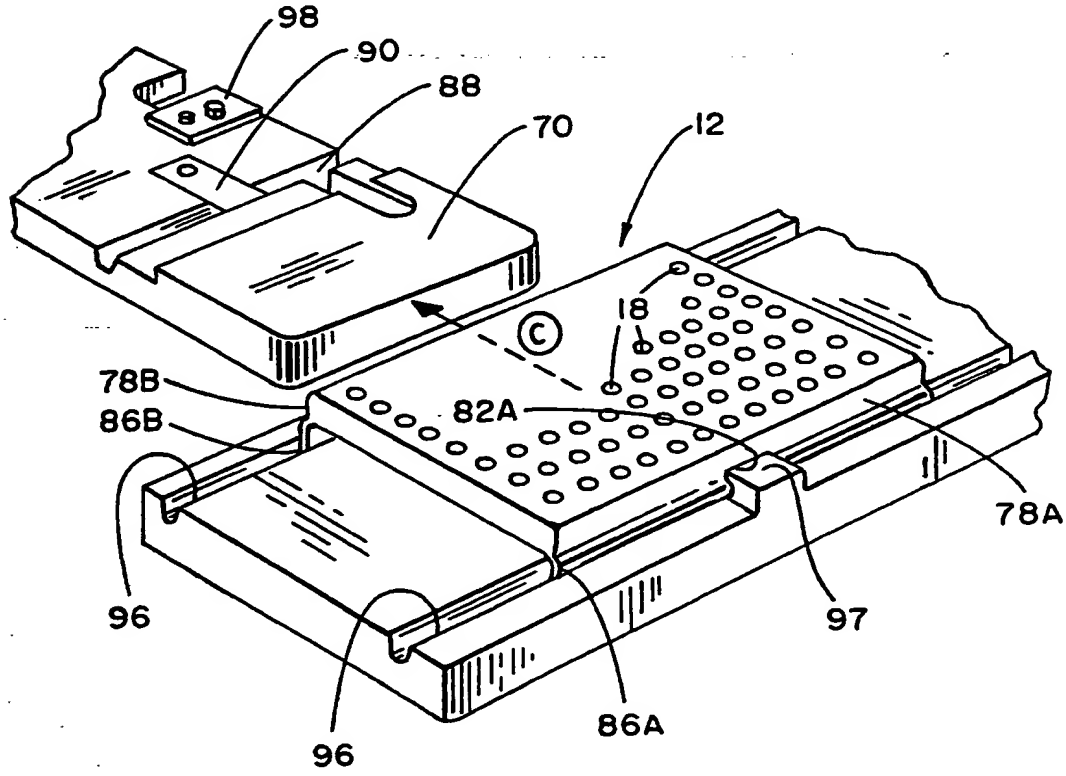

98
90
88
70
12
C
18
78B
86B
82A
78A
96
97
96
86A

FIG. 14

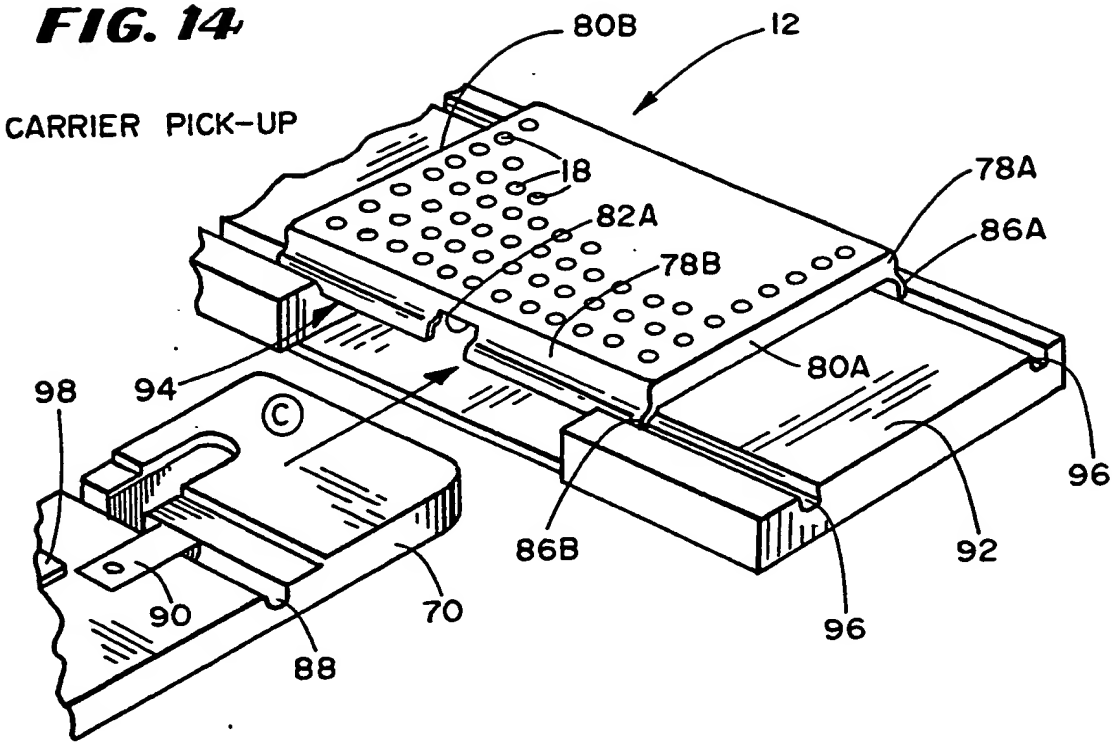

CARRIER PICK-UP
80B
12
18
78A
82A
86A
78B
80A
98
94
96
92
86B
90
70
96
88

FIG. 15

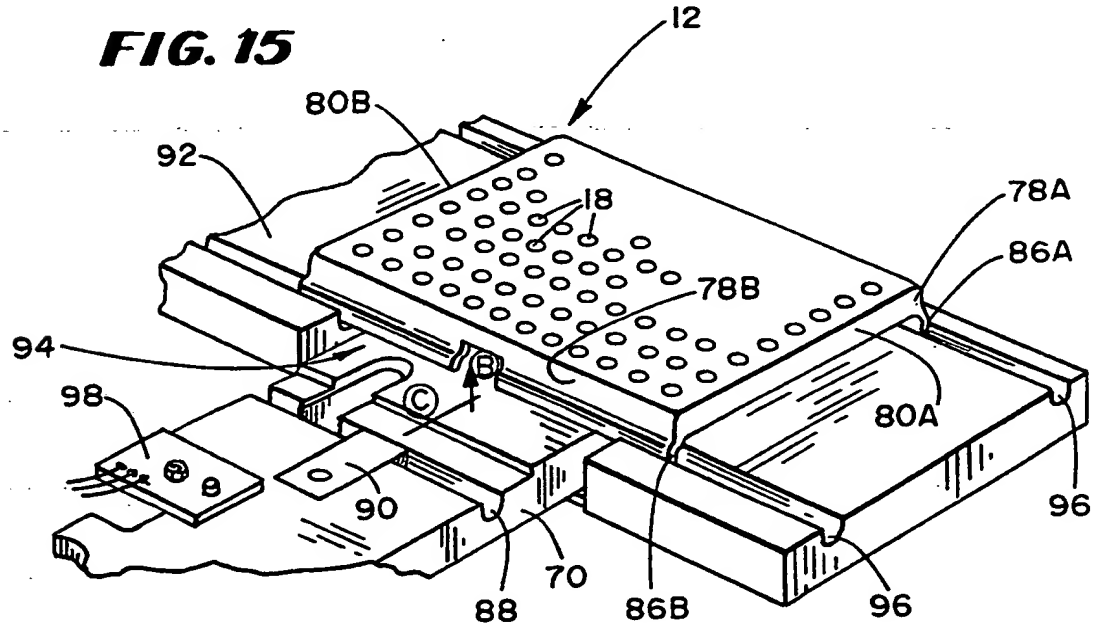

12
80B
92
18
78A
86A
78B
94
98
80A
90
96
70
88
86B
96

FIG. 16

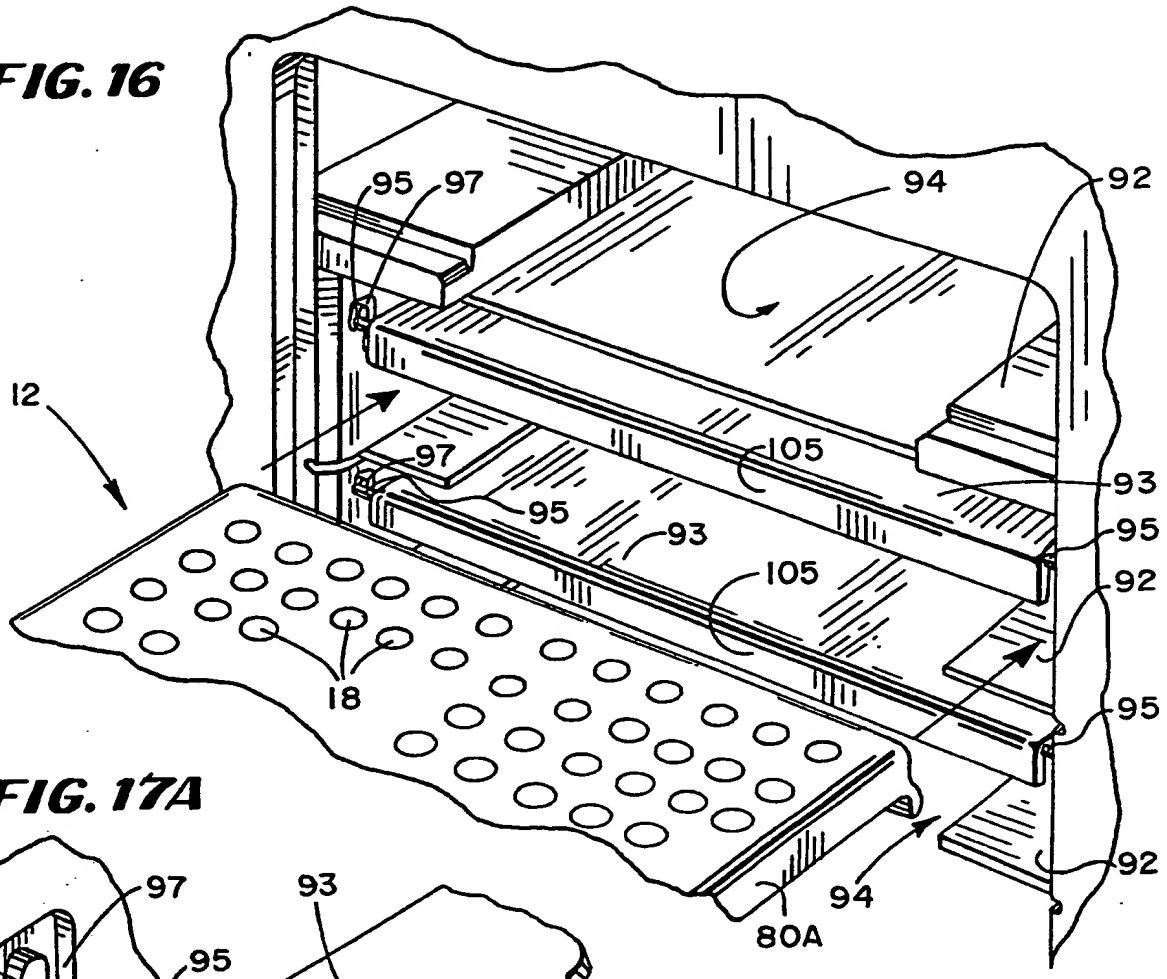


FIG. 17A

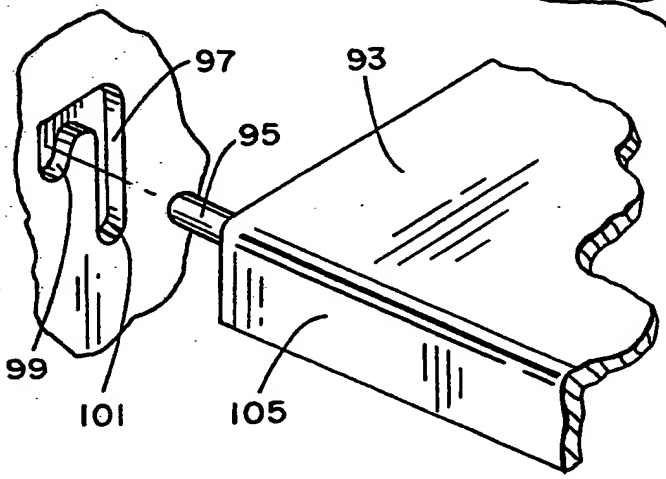


FIG. 17B

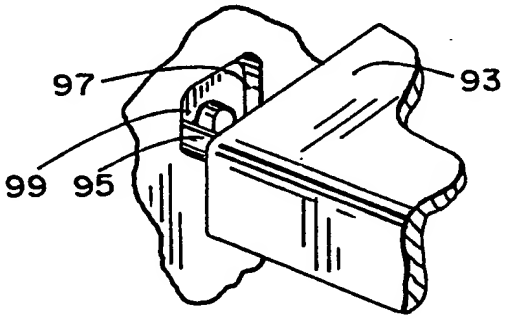


FIG. 18

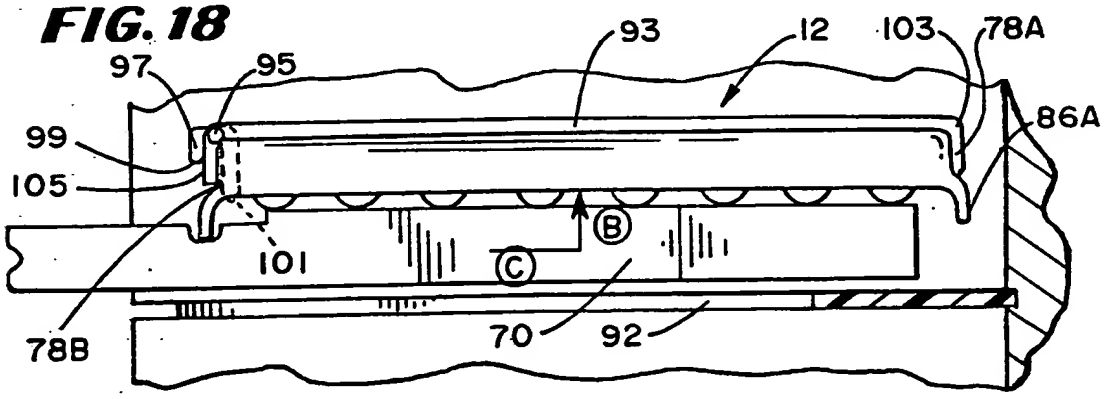


FIG. 19

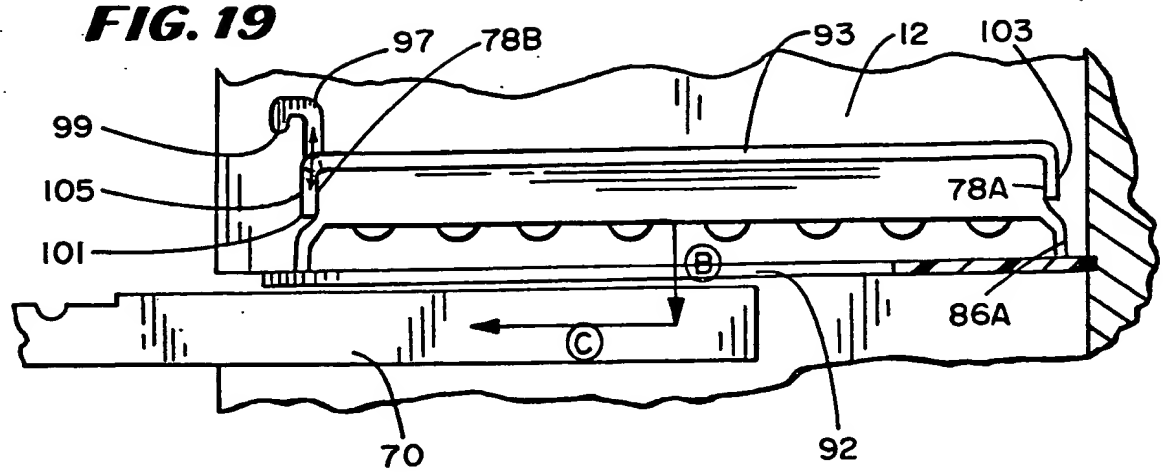


FIG. 20

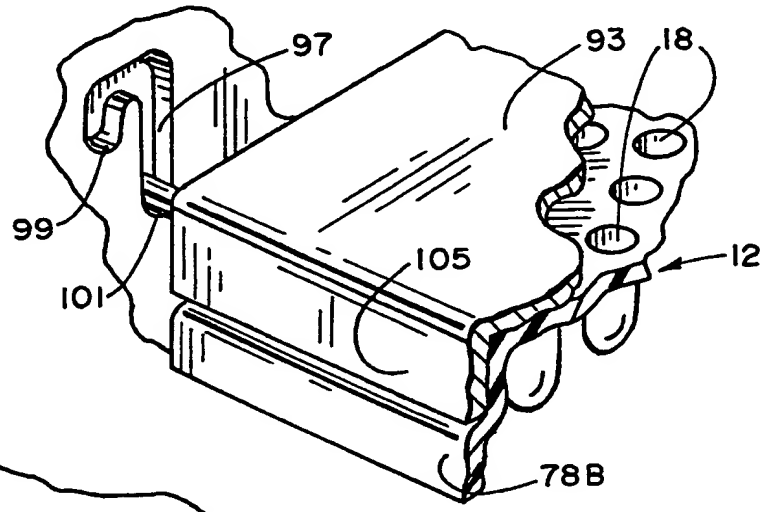


FIG. 21

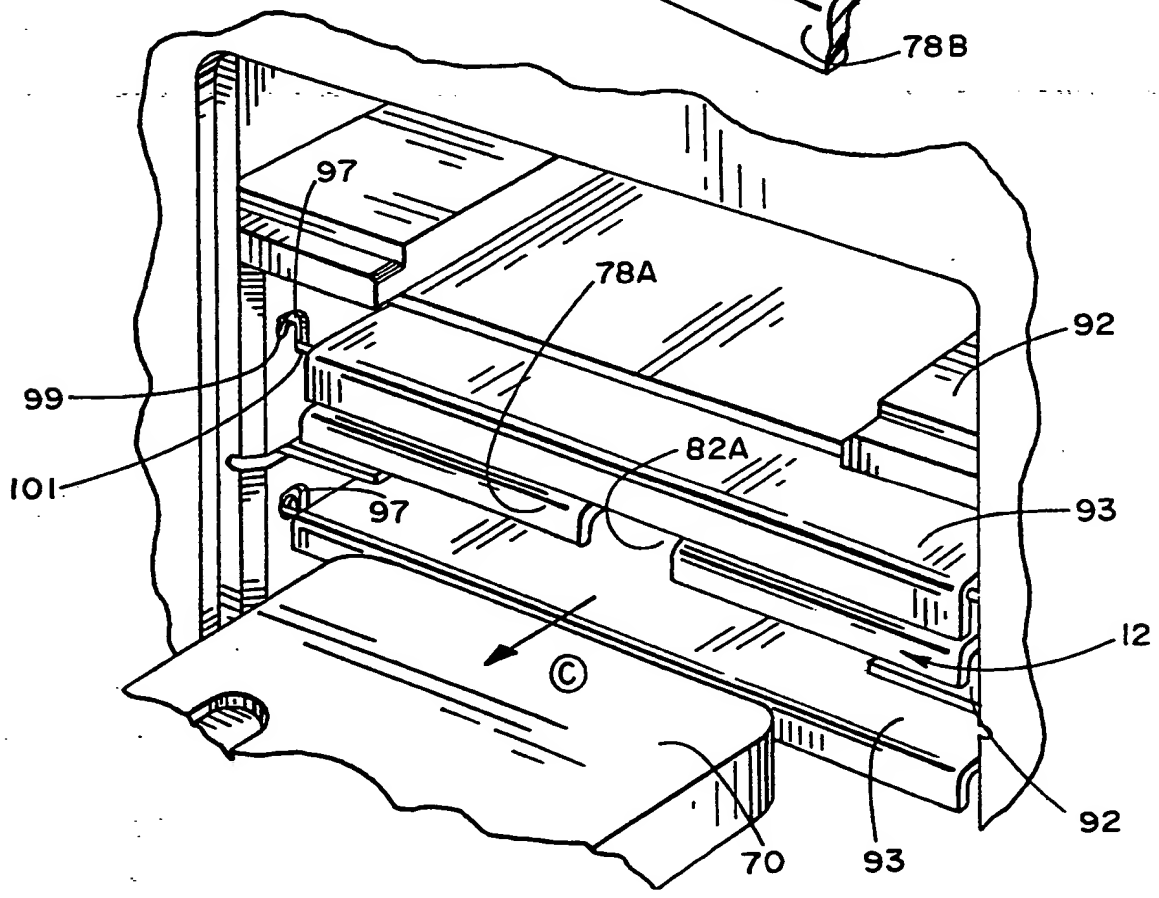
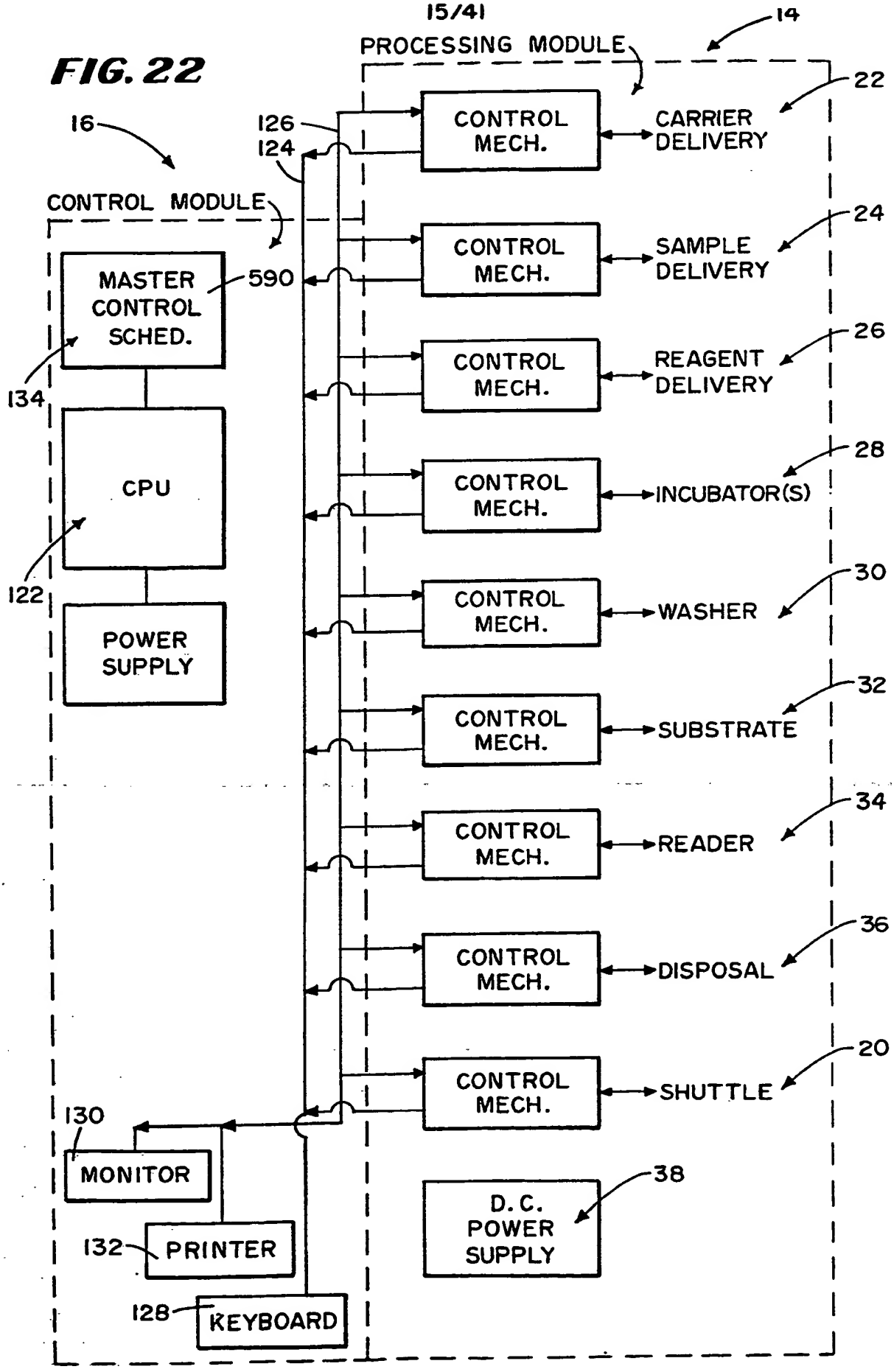


FIG. 22


PROCESSING MODULE
14
22
CONTROL MECH.
CARRIER DELIVERY
24
SAMPLE DELIVERY
26
REAGENT DELIVERY
28
INCUBATOR(S)
30
WASHER
32
SUBSTRATE
34
READER
36
DISPOSAL
20
SHUTTLE
38
D.C. POWER SUPPLY
16
CONTROL MODULE
126
124
590
MASTER CONTROL SCHED.
134
CPU
122
POWER SUPPLY
130
MONITOR
132
PRINTER
128
KEYBOARD

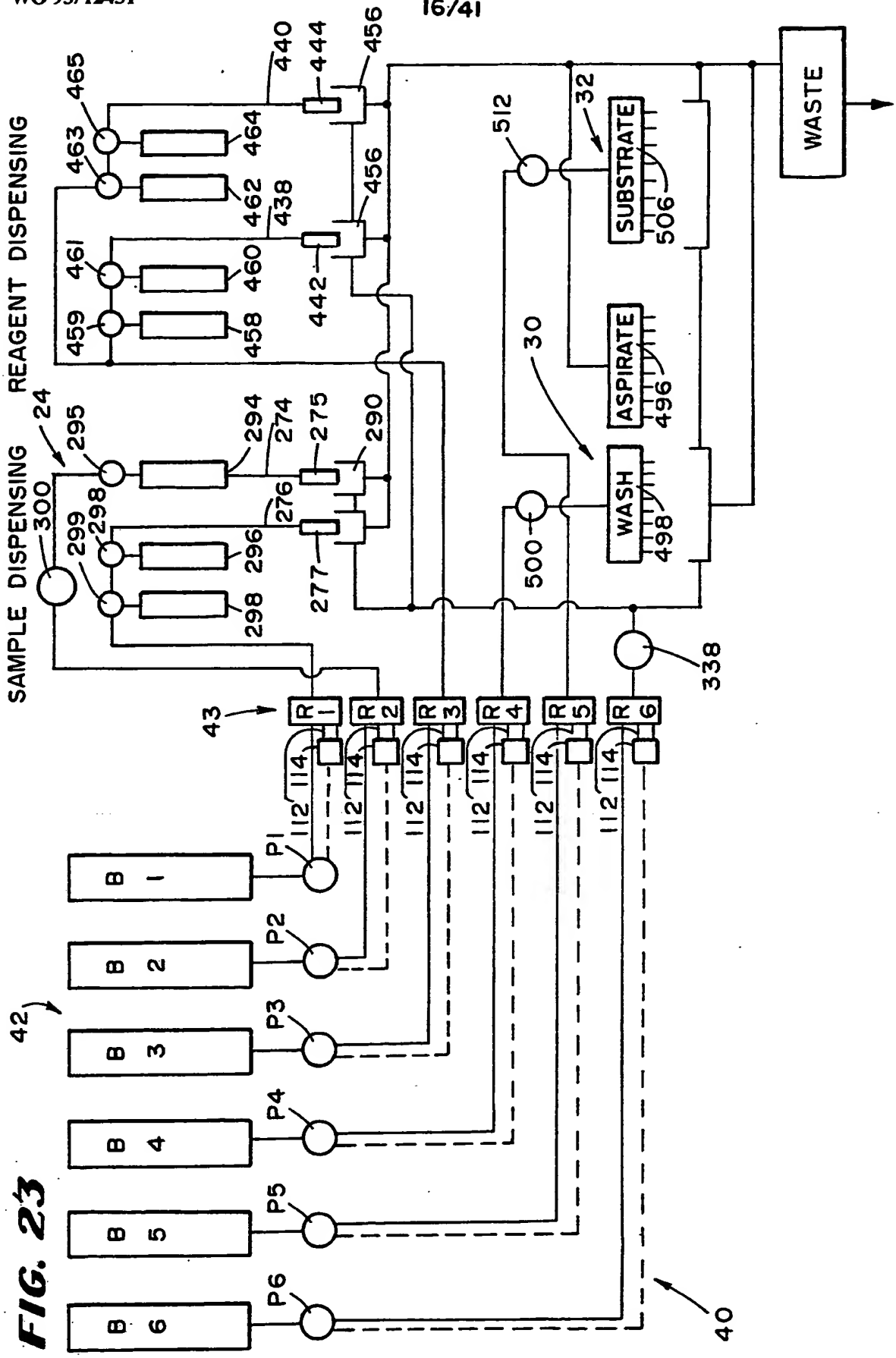

REAGENT DISPENSING
SAMPLE DISPENSING
WASTE
SUBSTRATE
ASPIRATE
WASH
B 1
B 2
B 3
B 4
B 5
B 6
R 1
R 2
R 3
R 4
R 5
R 6
P1
P2
P3
P4
P5
P6
24
30
32
40
42
43
338
440
444
456
438
442
460
462
464
465
463
461
459
458
274
275
276
277
290
294
295
296
298
299
300
500
506
512
496
498
112
114

FIG. 23

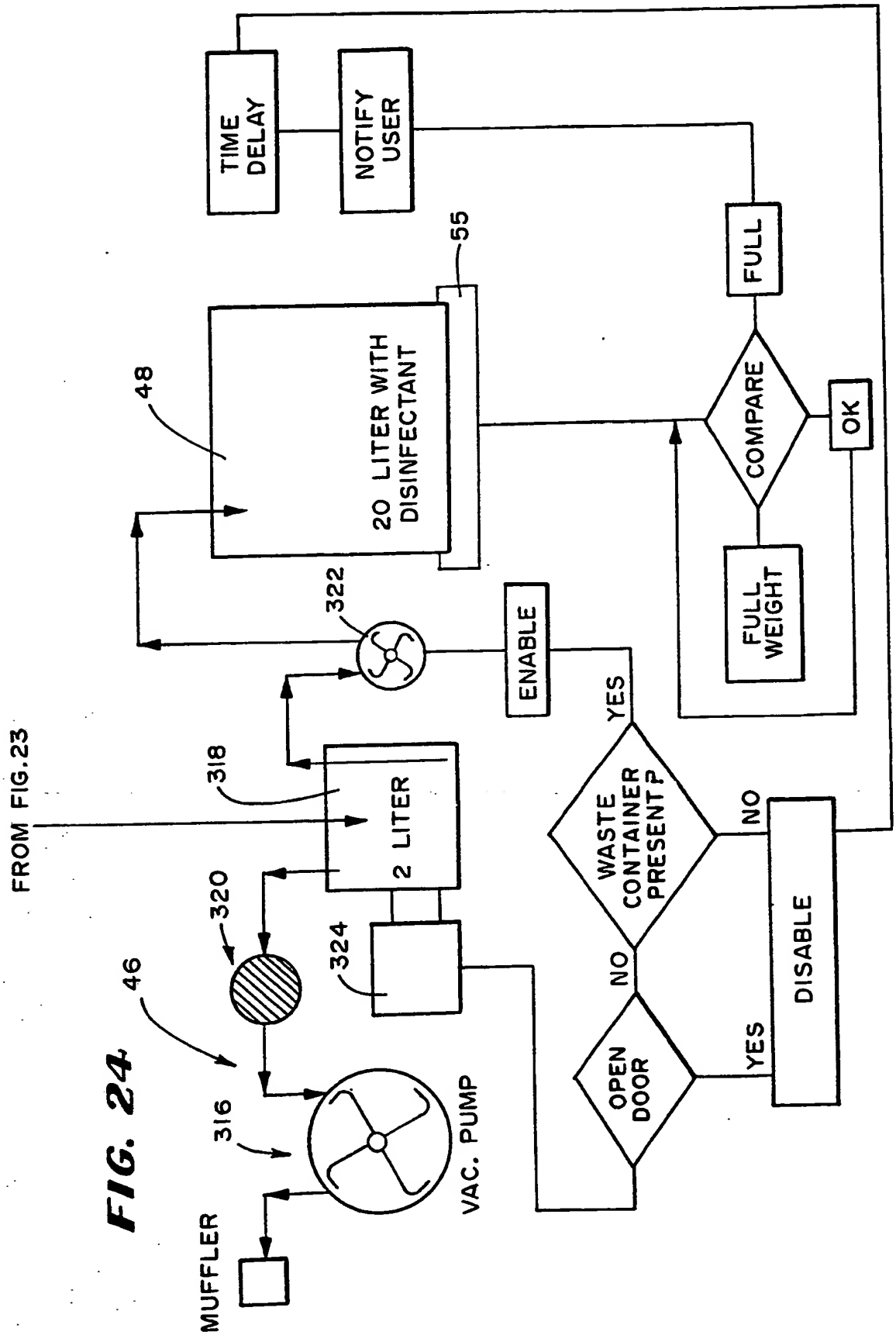

TIME DELAY
NOTIFY USER
55
FULL
48
20 LITER WITH DISINFECTANT
COMPARE
OK
FULL WEIGHT
322
ENABLE
YES
FROM FIG. 23
318
2 LITER
WASTE CONTAINER PRESENT?
NO
DISABLE
320
324
NO
46
OPEN DOOR
YES
316
VAC. PUMP
MUFFLER

FIG. 24

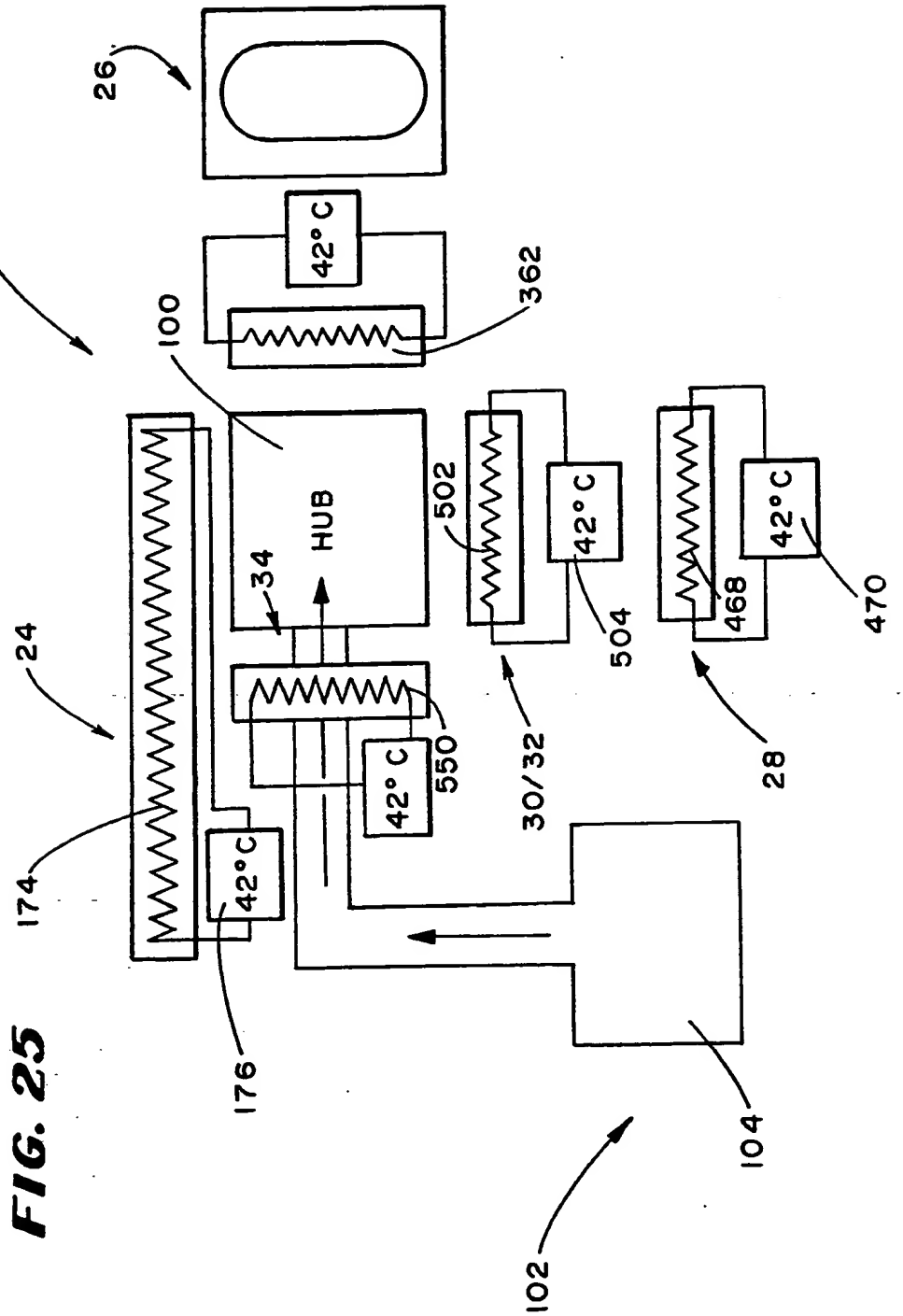

26
52
42° C
362
100
HUB
34
502
42° C
504
468
42° C
470
24
550
42° C
30/32
28
174
42° C
176
102
104

FIG. 25

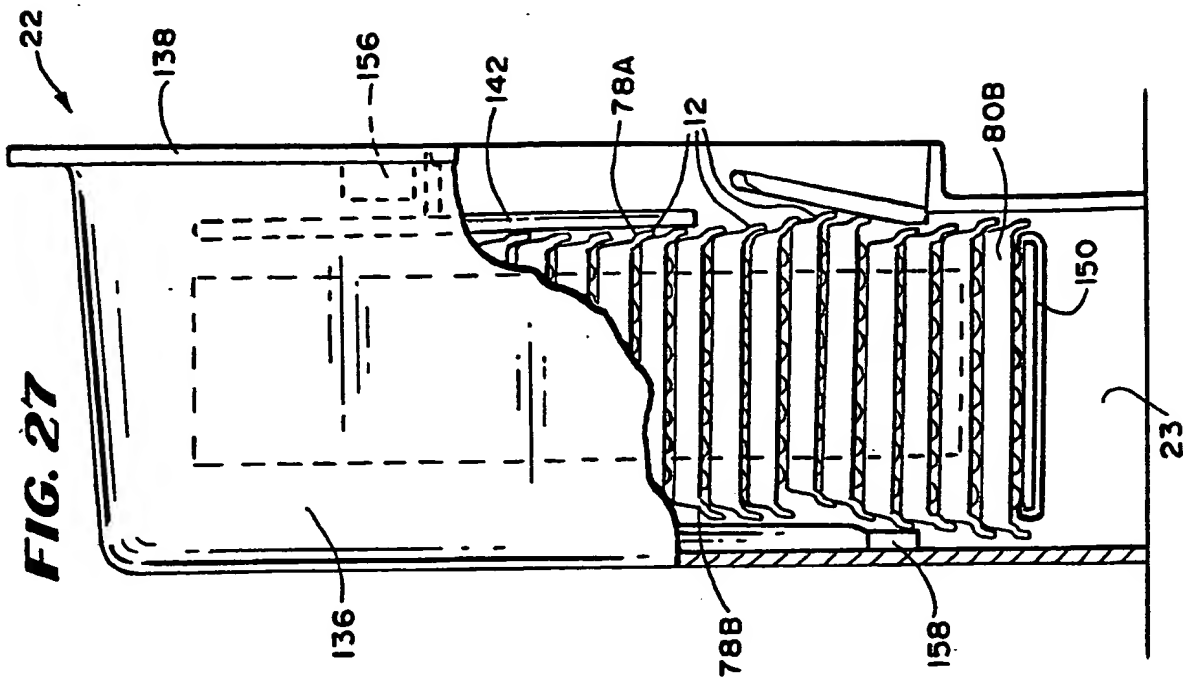

22
138
156
142
78A
12
808
150
23
136
78B
158

FIG. 27

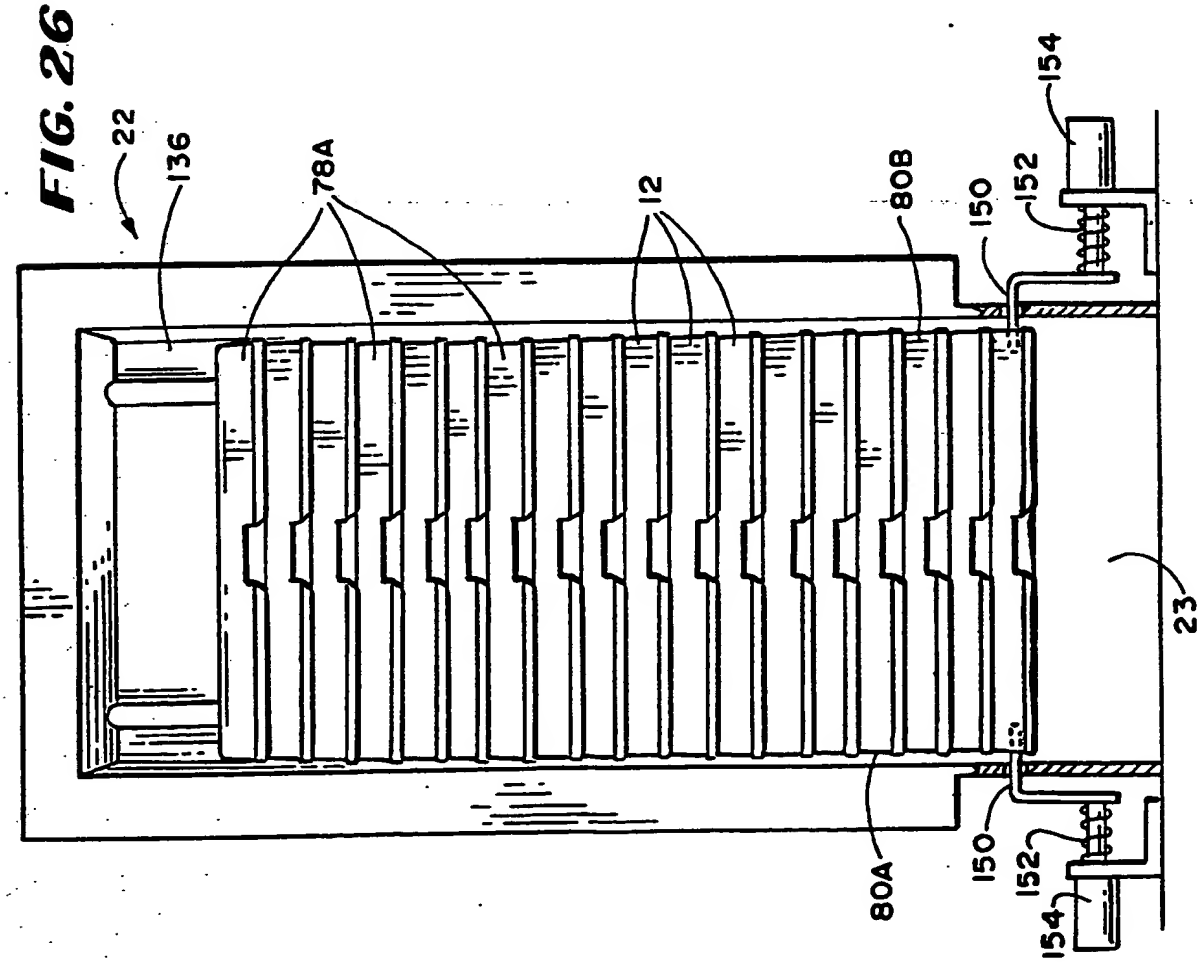

22
136
78A
12
808
150
152
154
23
80A
150
152
154

FIG. 26

FIG. 28

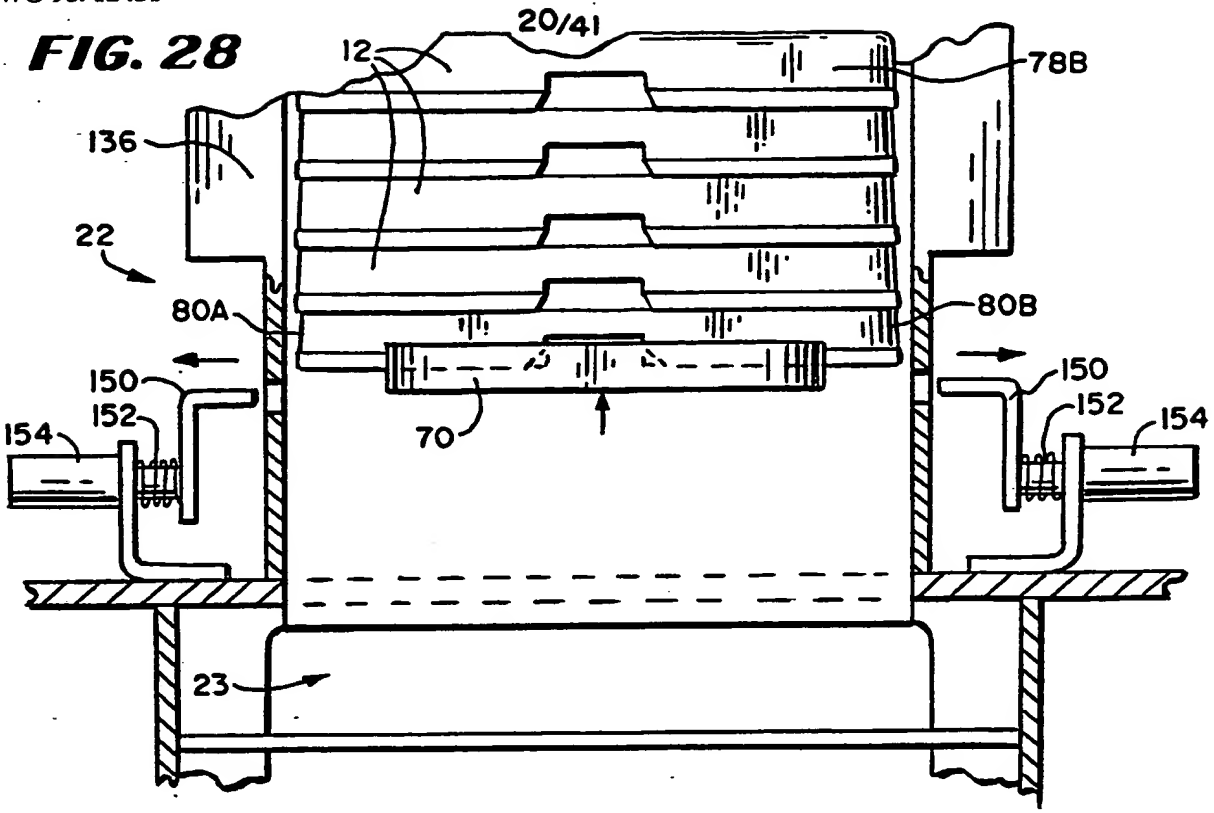

20/41
12
78B
136
22
80A
80B
150
150
152
154
154
152
70
23

FIG. 29

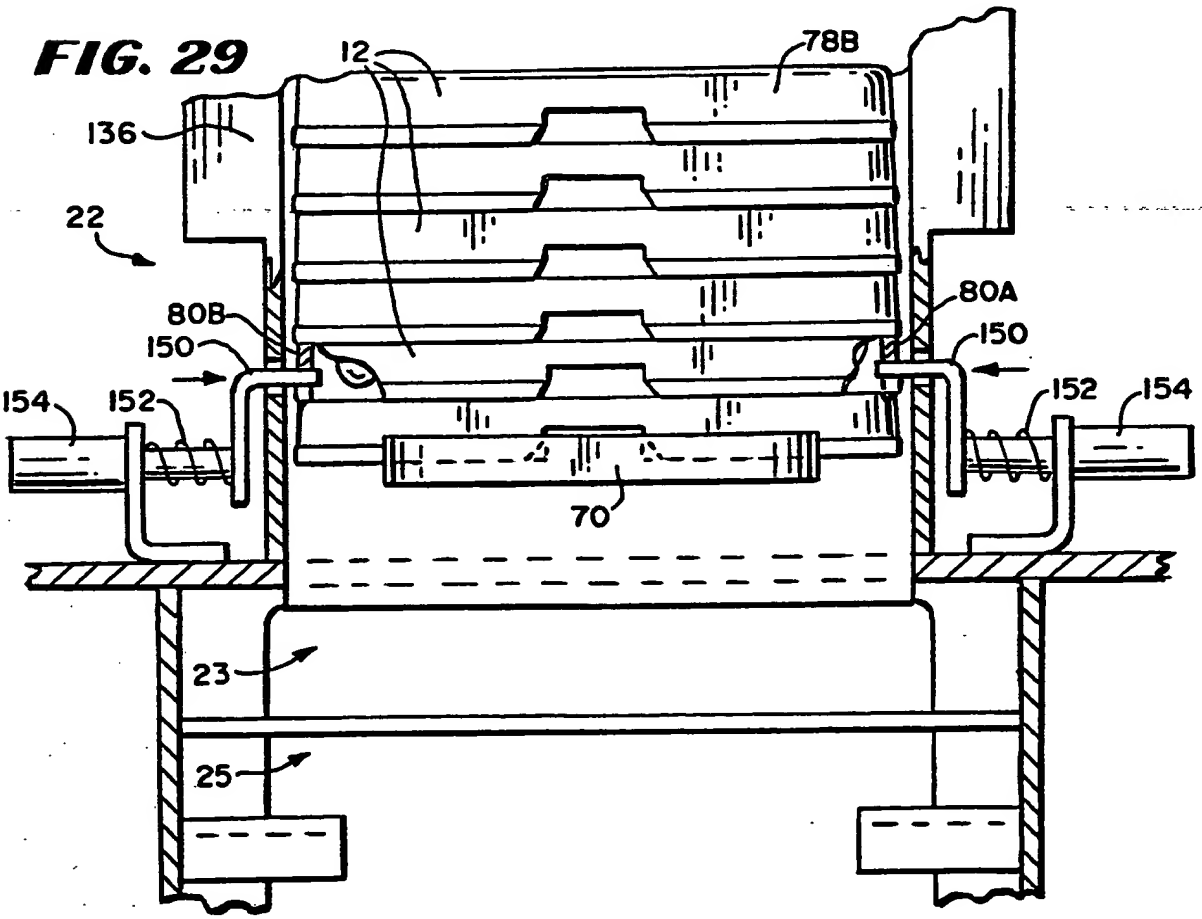

12
78B
136
22
80B
80A
150
150
154
152
152
154
70
23
25

FIG. 30

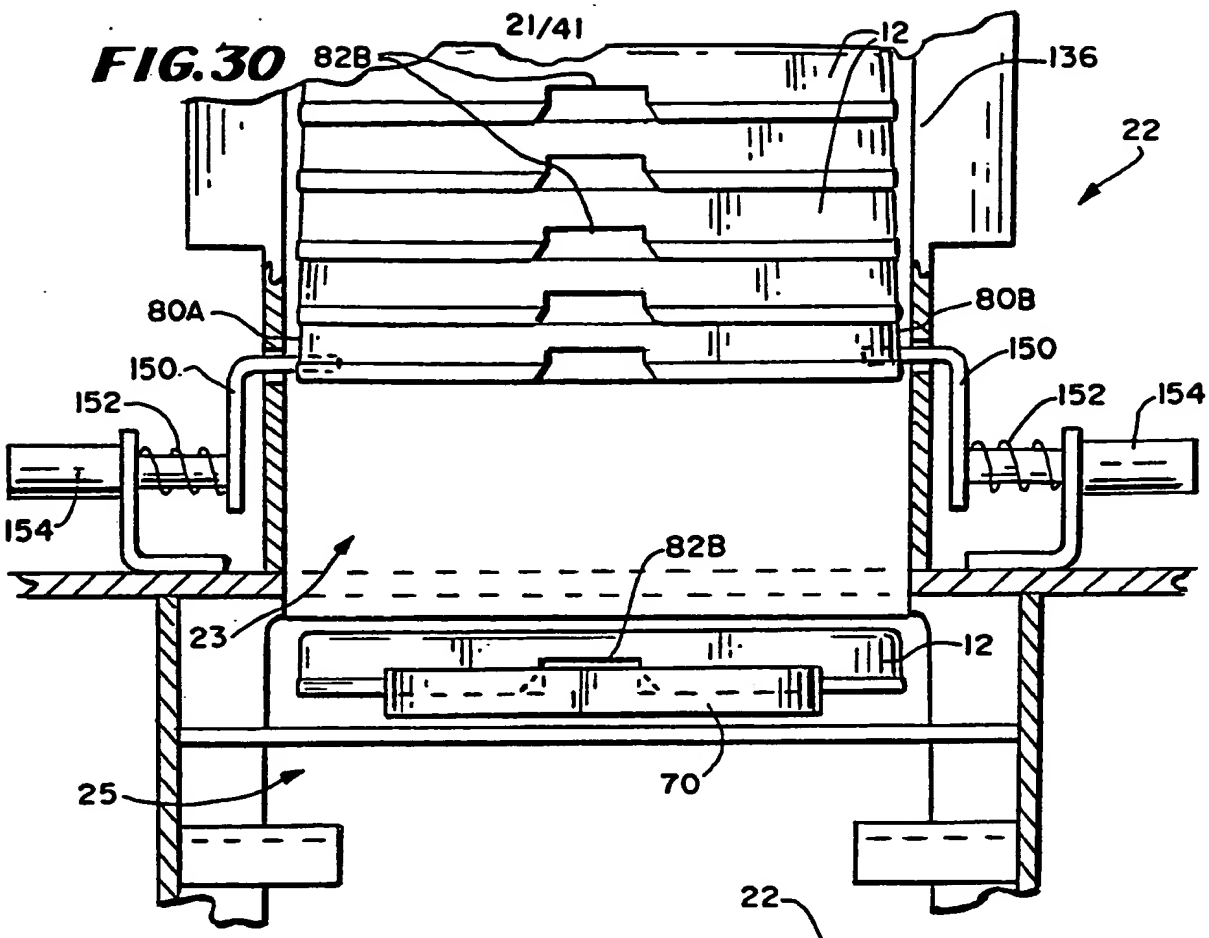
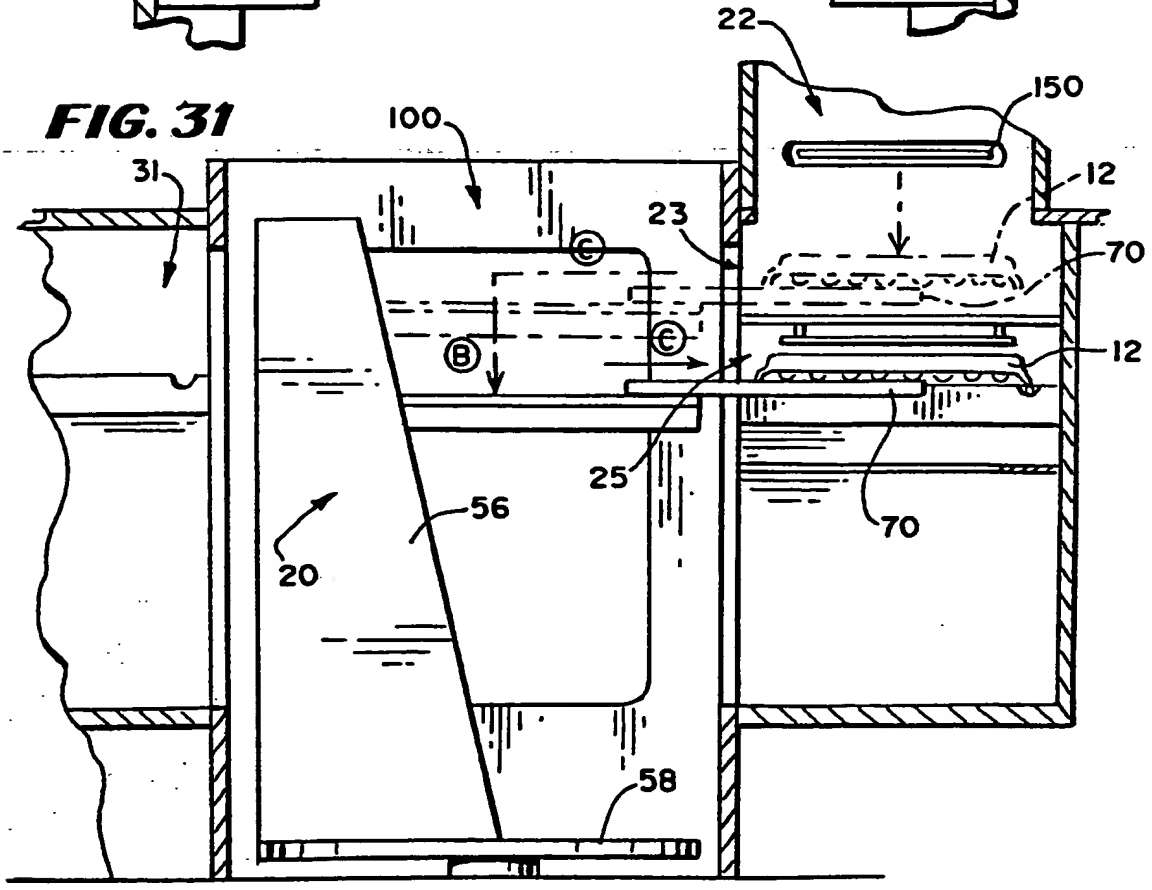

21/41
828
12
136
22
80A
80B
150
150
152
152
154
154
828
23
12
25
70

FIG. 31


22
150
100
31
12
23
70
12
25
56
70
20
58

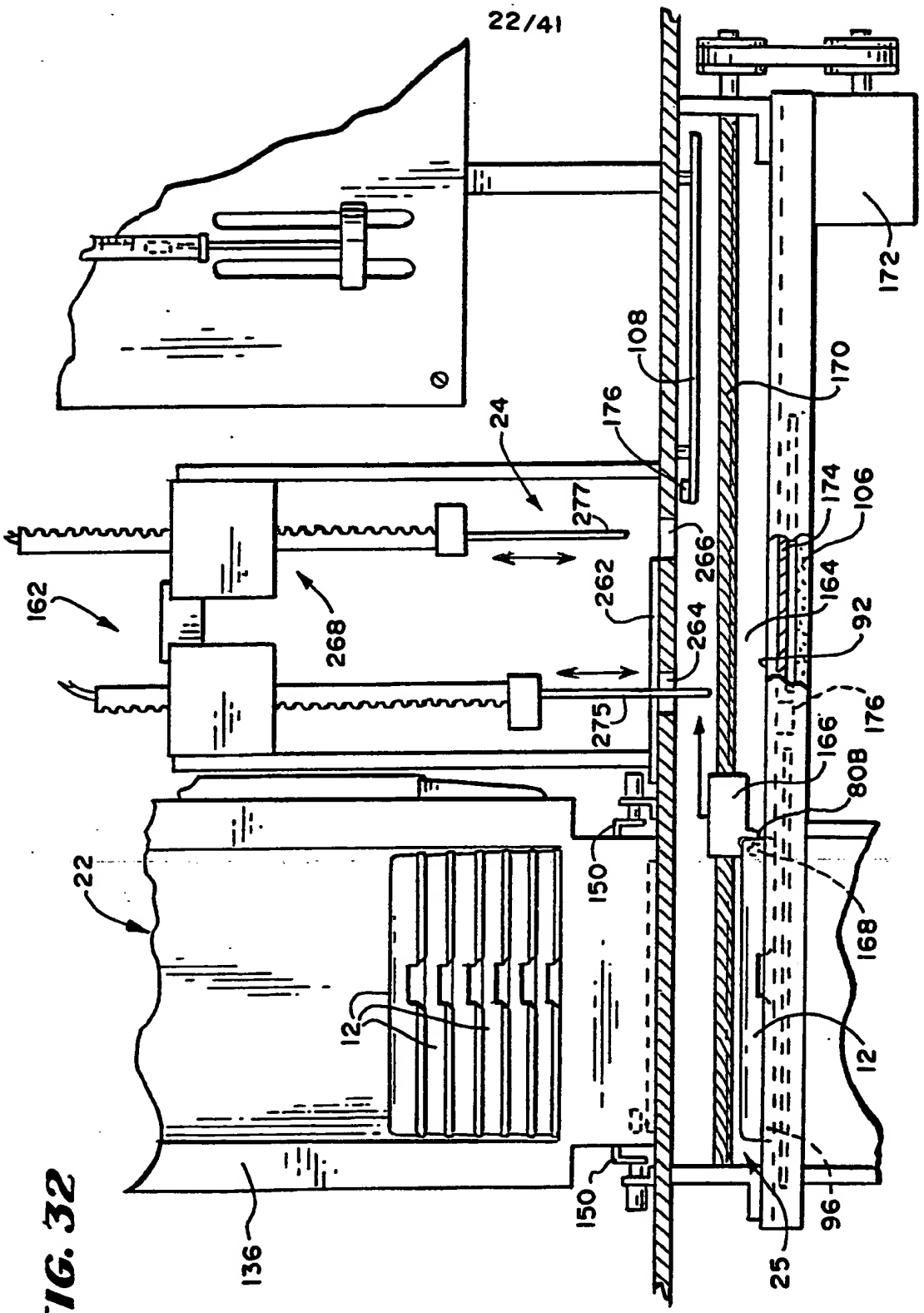

172
108
170
176
24
277
174
106
266
262
164
162
268
264
92
275
166
176
808
150
22
168
12
12
150
96
136
25

FIG. 32

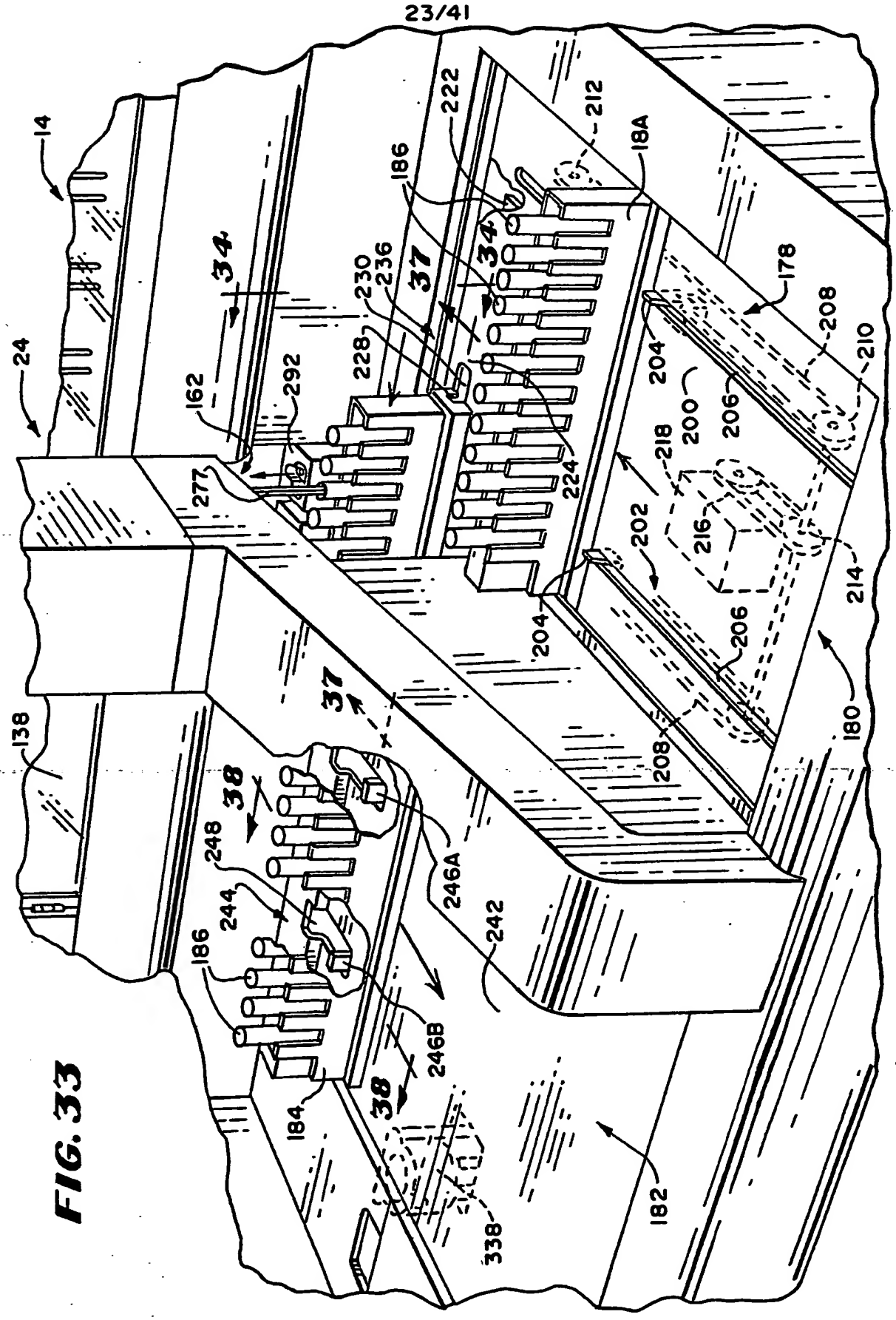

14
24
34
34
37
37
38
38
37
162
292
277
186
222
212
18A
230
236
228
224
178
208
210
204
200
206
218
216
202
214
204
206
208
180
138
248
244
186
246A
242
246B
184
338
182

FIG. 33

FIG. 34

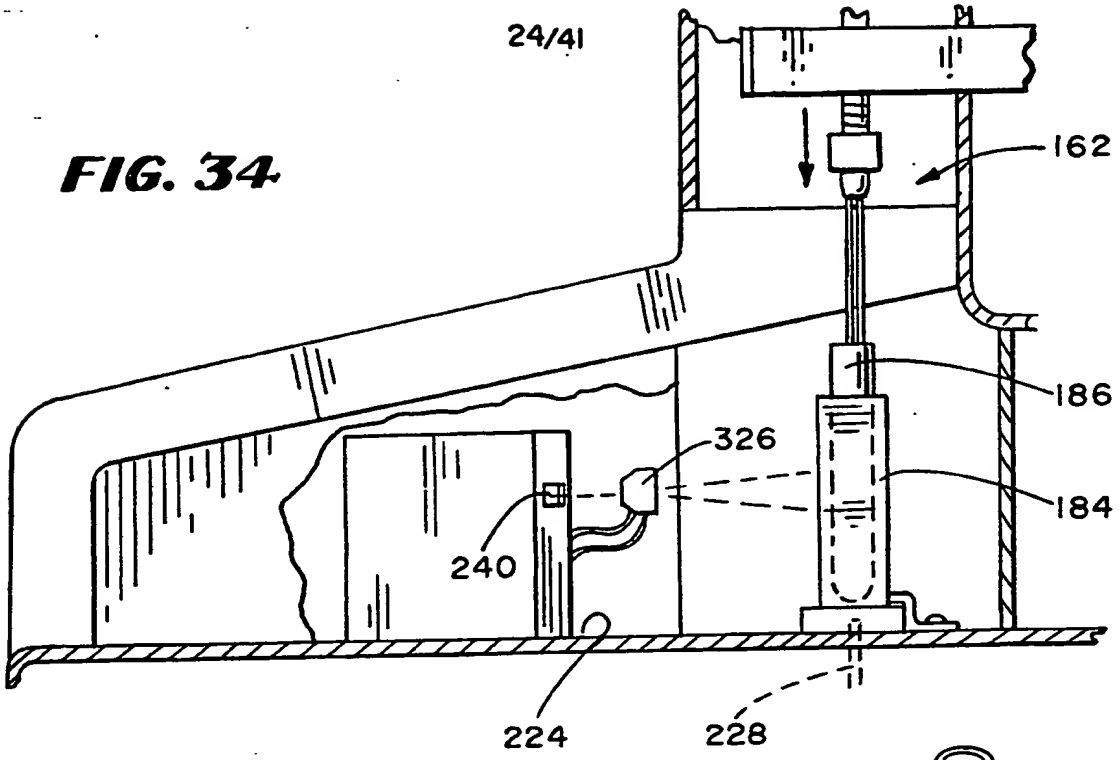


FIG. 35

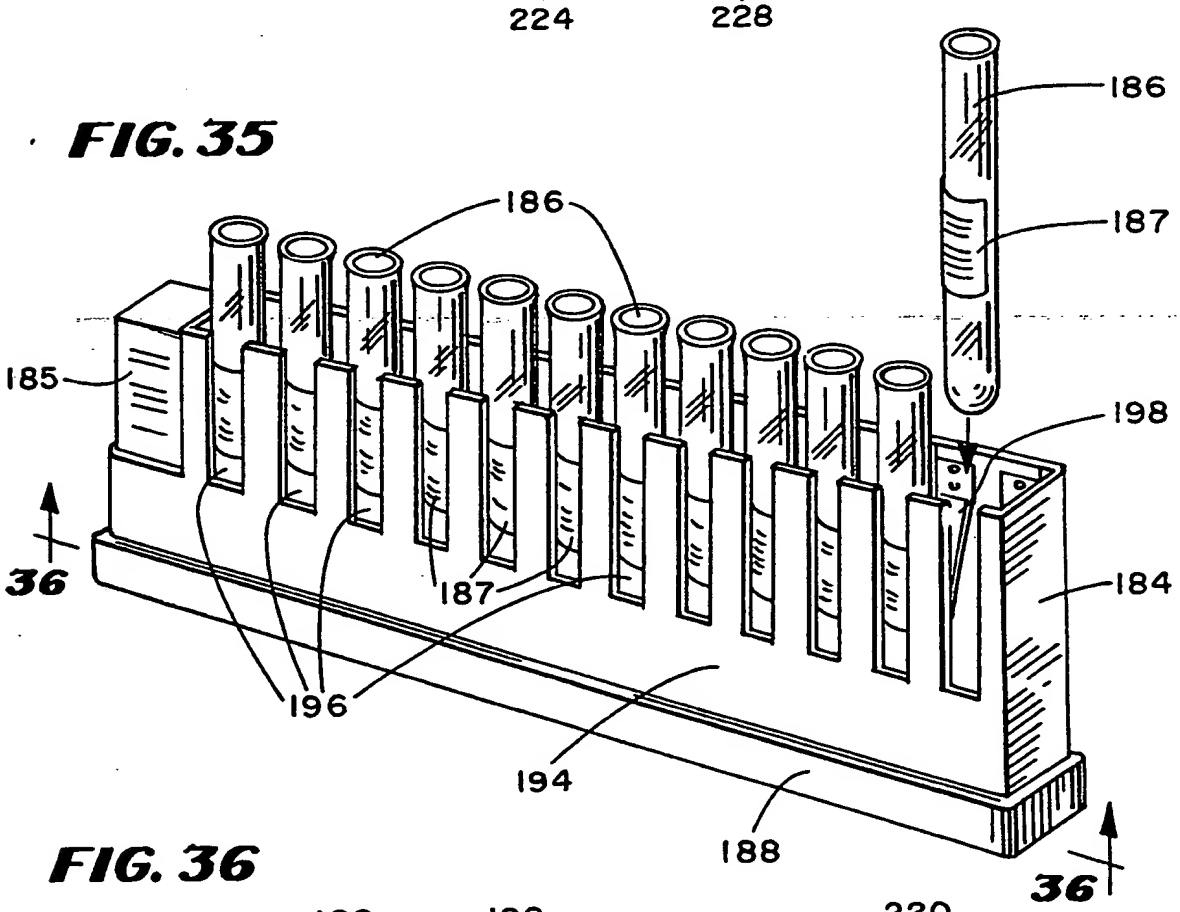


FIG. 36

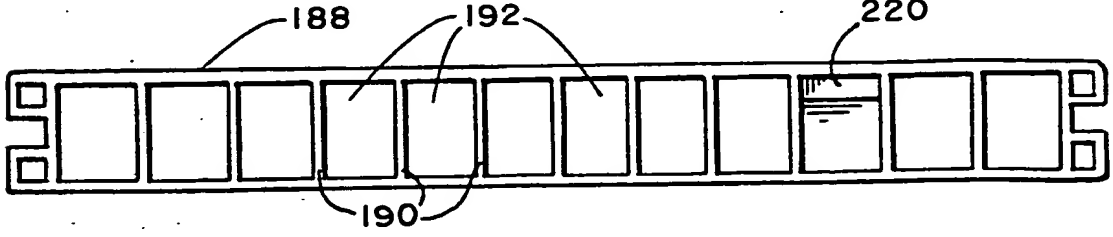


FIG. 37

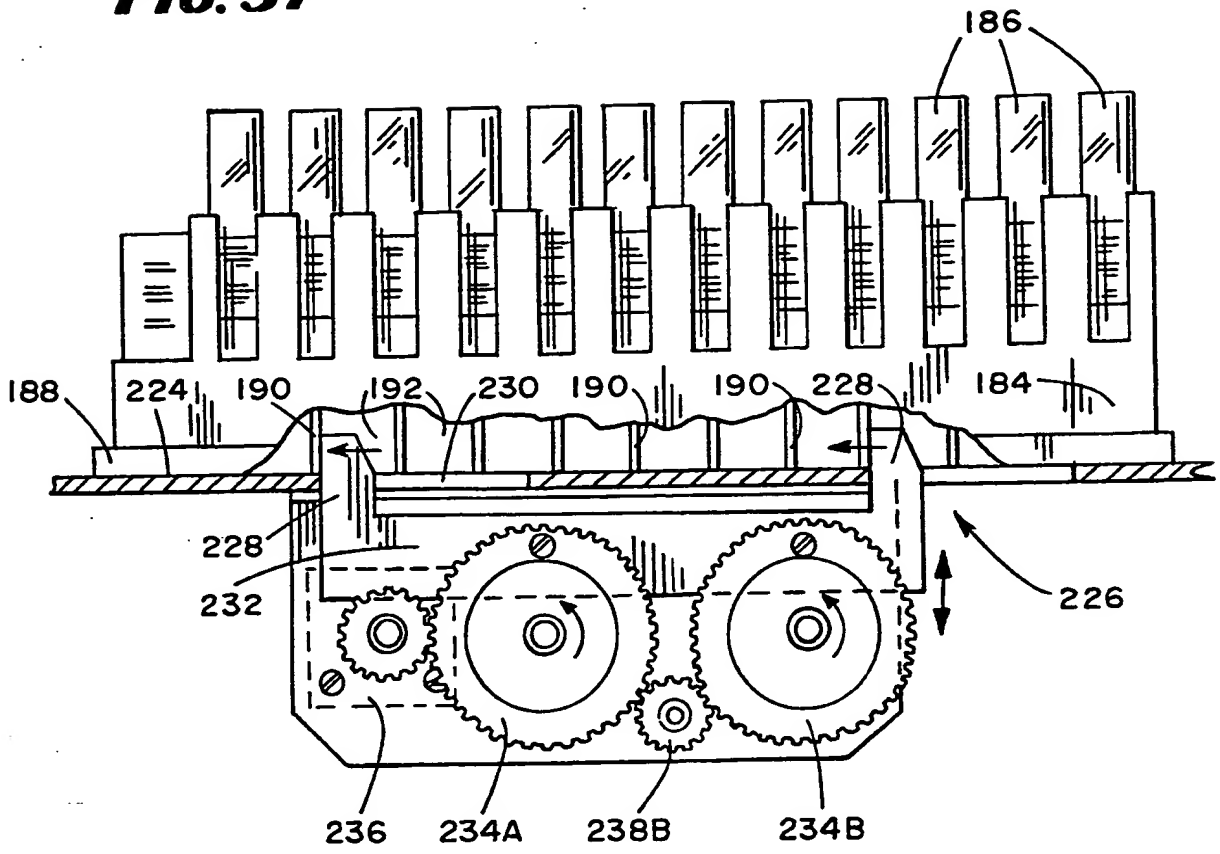
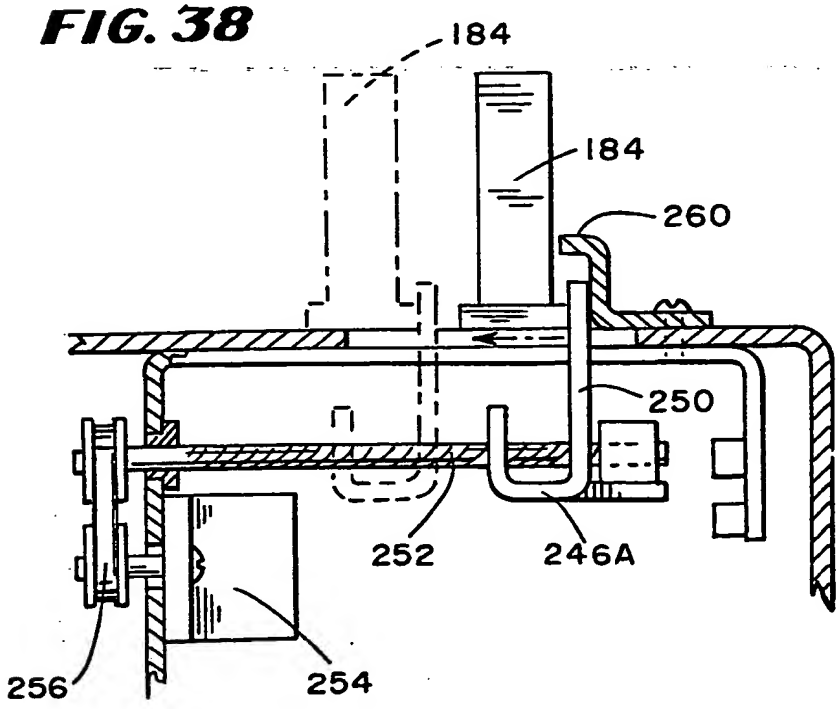

186
188
224
190
192
230
190
190
228
184
228
232
226
236
234A
238B
234B

FIG. 38


184
184
260
250
252
246A
256
254

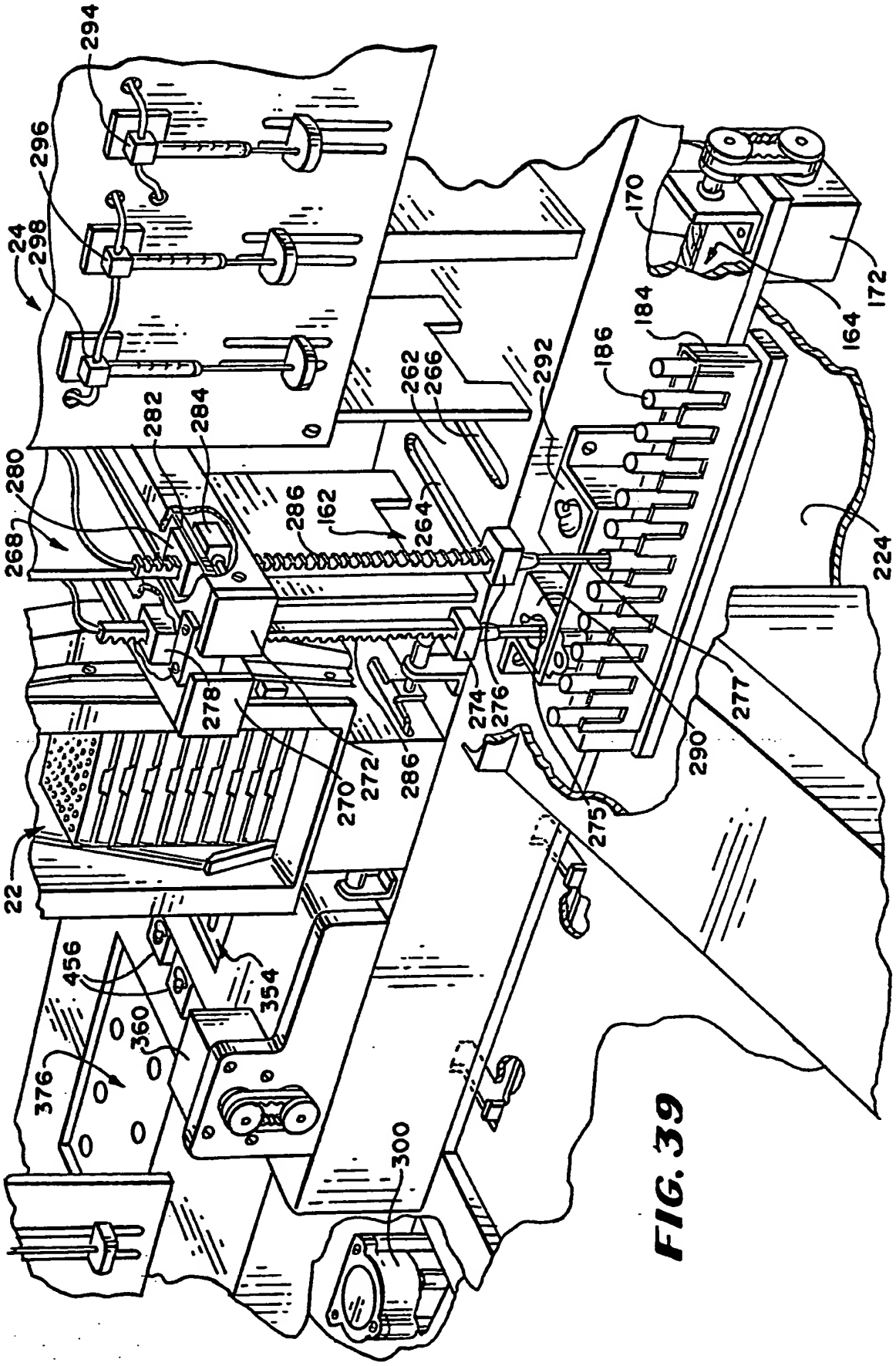
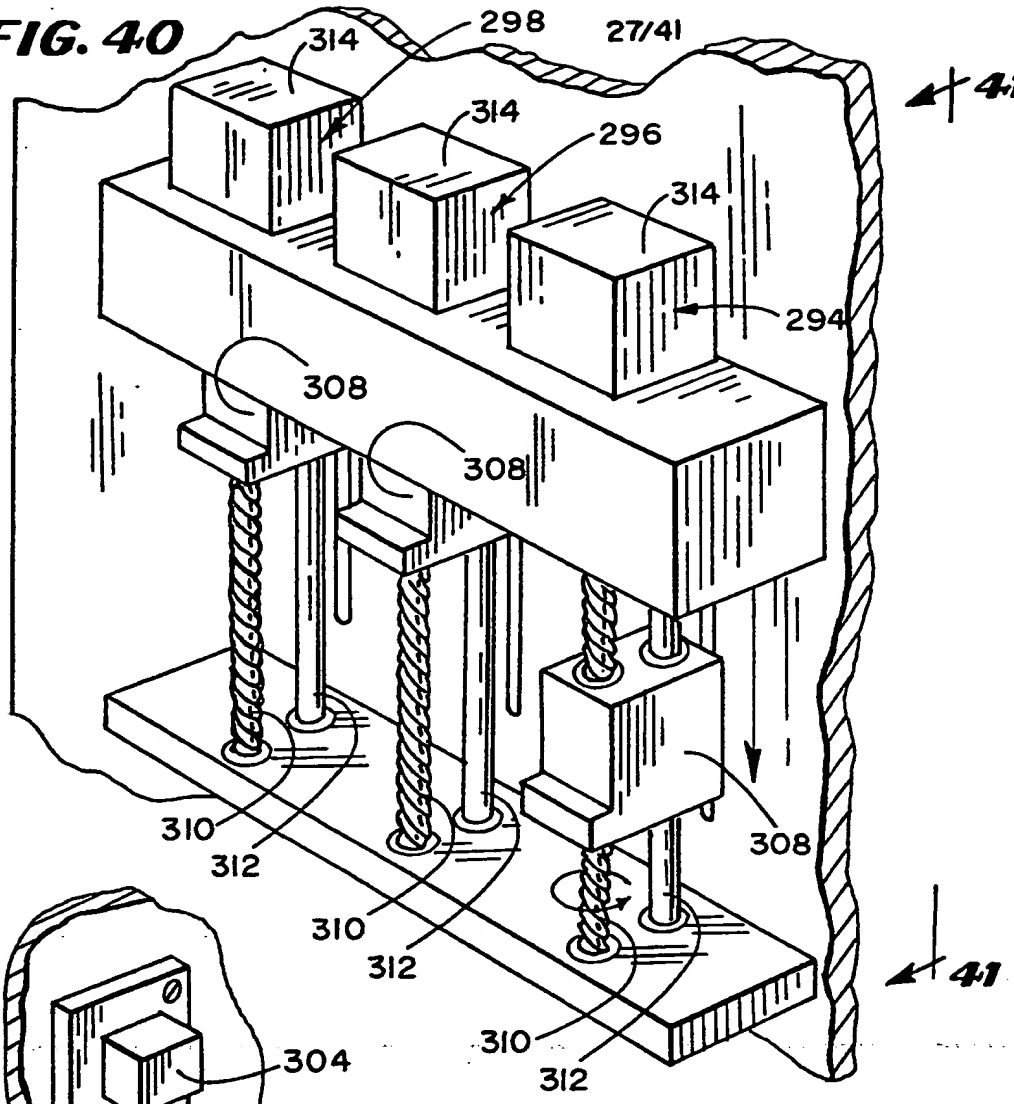

294
296
24
298
282
284
280
268
262
266
292
186
184
170
172
164
162
286
264
224
278
274
276
277
290
270
272
286
275
22
456
354
360
376
300

FIG. 39

FIG. 40


298
27/41
314
314
296
314
294
308
308
310
312
310
312
310
312
308
41
41

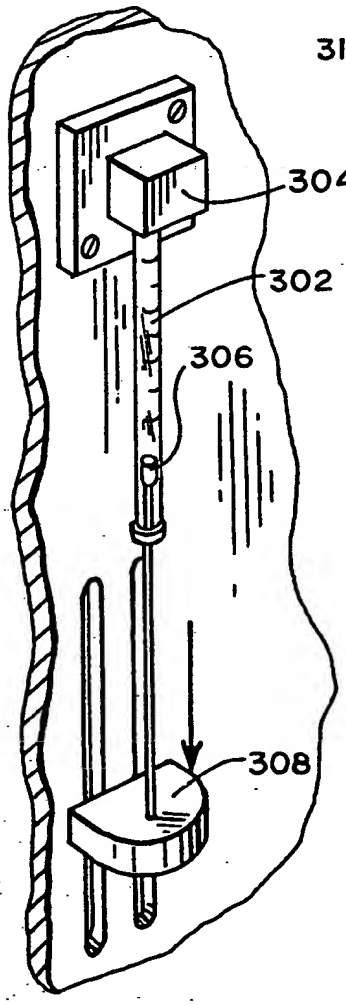

304
302
306
308

FIG. 41

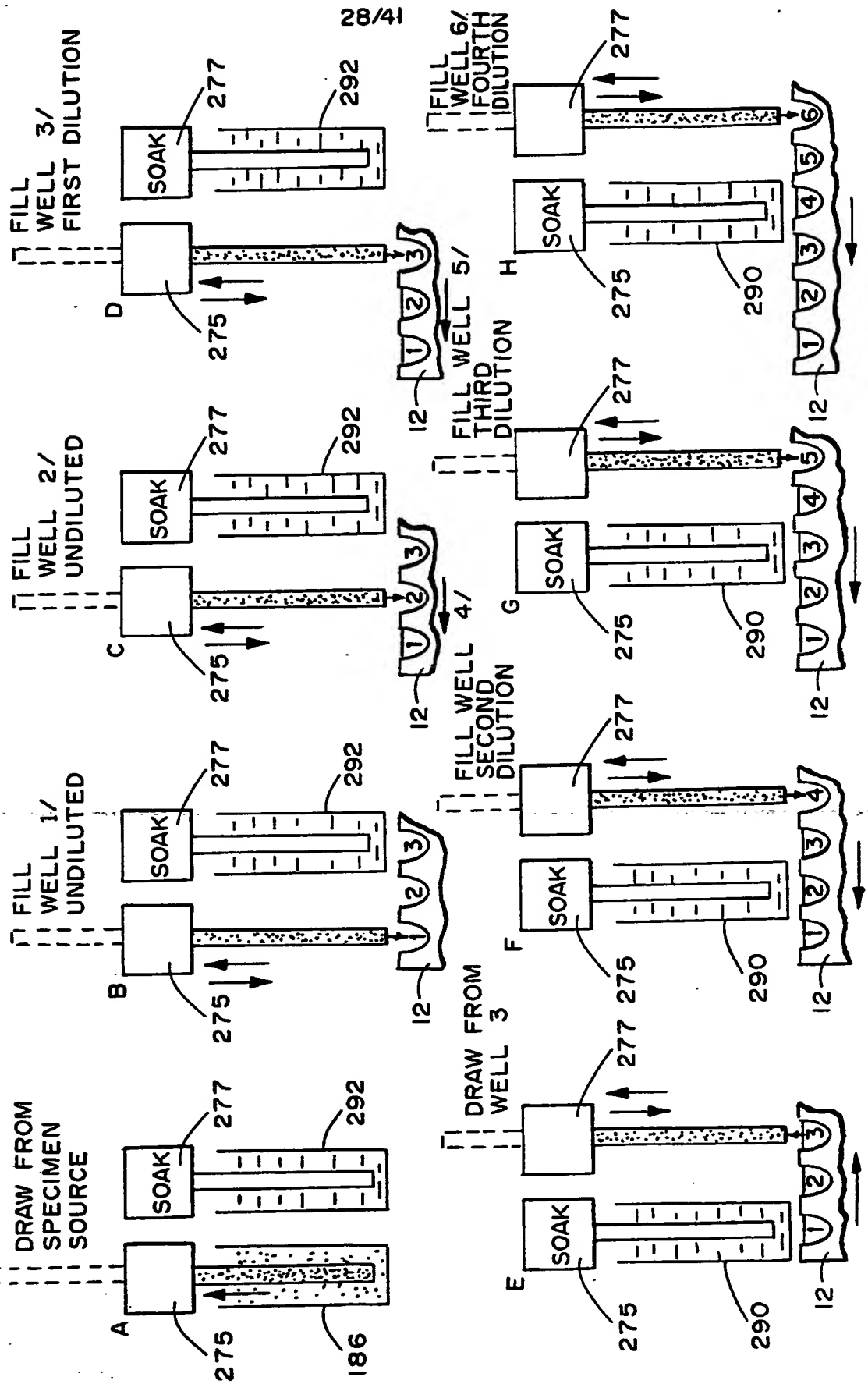

DRAW FROM SPECIMEN SOURCE
FILL WELL 1/ UNDILUTED
FILL WELL 2/ UNDILUTED
FILL WELL 3/ FIRST DILUTION
FILL WELL 4/ SECOND DILUTION
FILL WELL 5/ THIRD DILUTION
FILL WELL 6/ FOURTH DILUTION
DRAW FROM WELL 3
SOAK
A
B
C
D
E
F
G
H
275
277
290
292
186
12
1
2
3
4
5
6

FIG. 42

FIG. 43

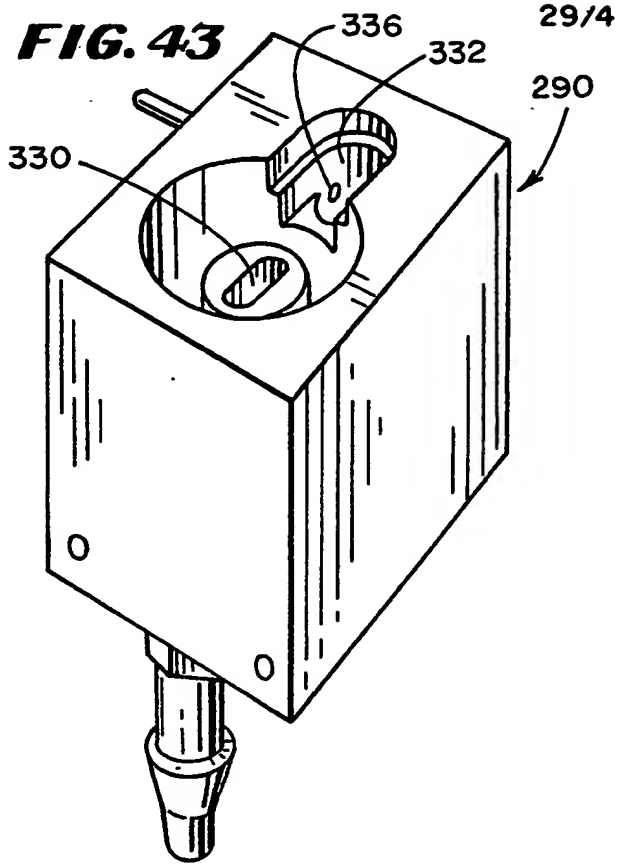


FIG. 44

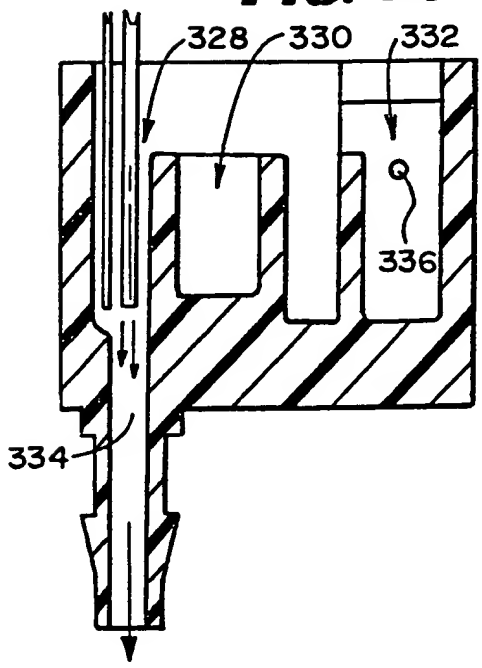


FIG. 45

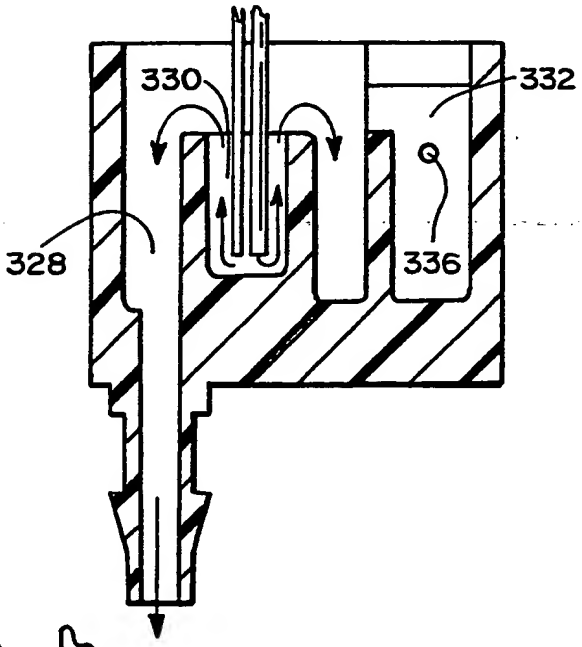


FIG. 46

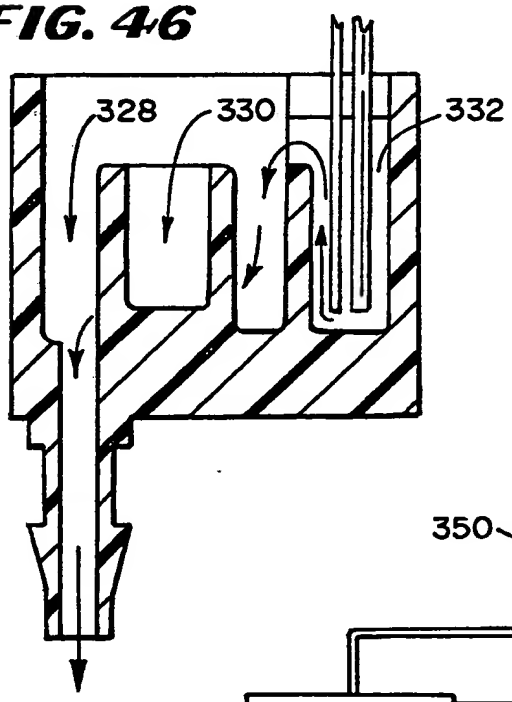
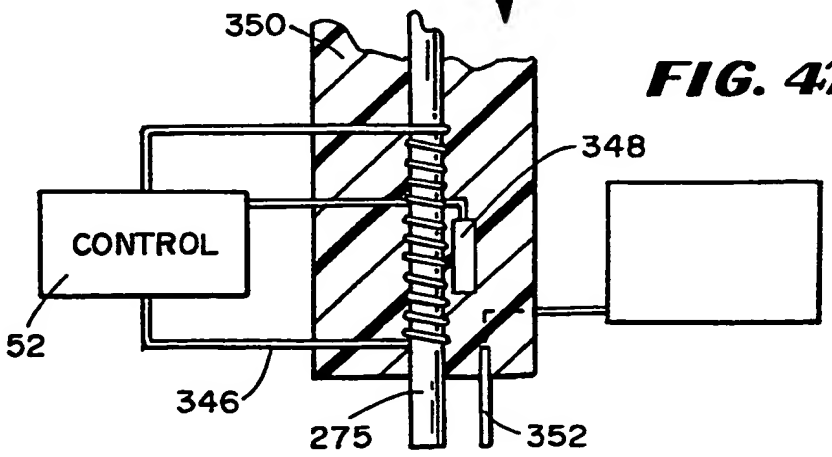


FIG. 47



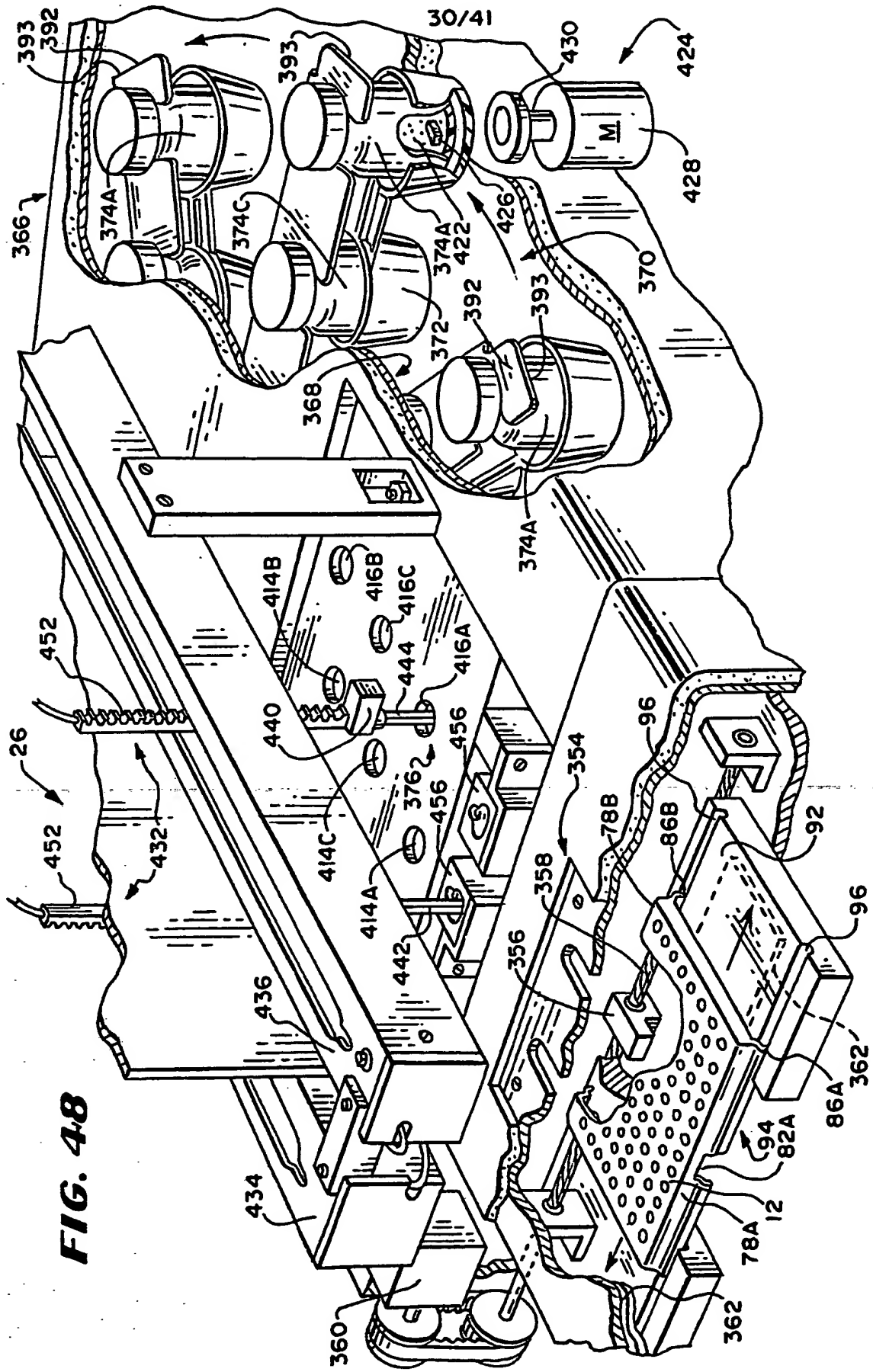

30/41
393
392
374A
374C
366
368
372
370
374A
422
426
428
424
430
M
452
26
432
414B
416B
416C
416A
444
440
414C
376
456
414A
442
436
434
360
354
358
356
78B
86B
92
96
362
86A
94
82A
12
78A

FIG. 48

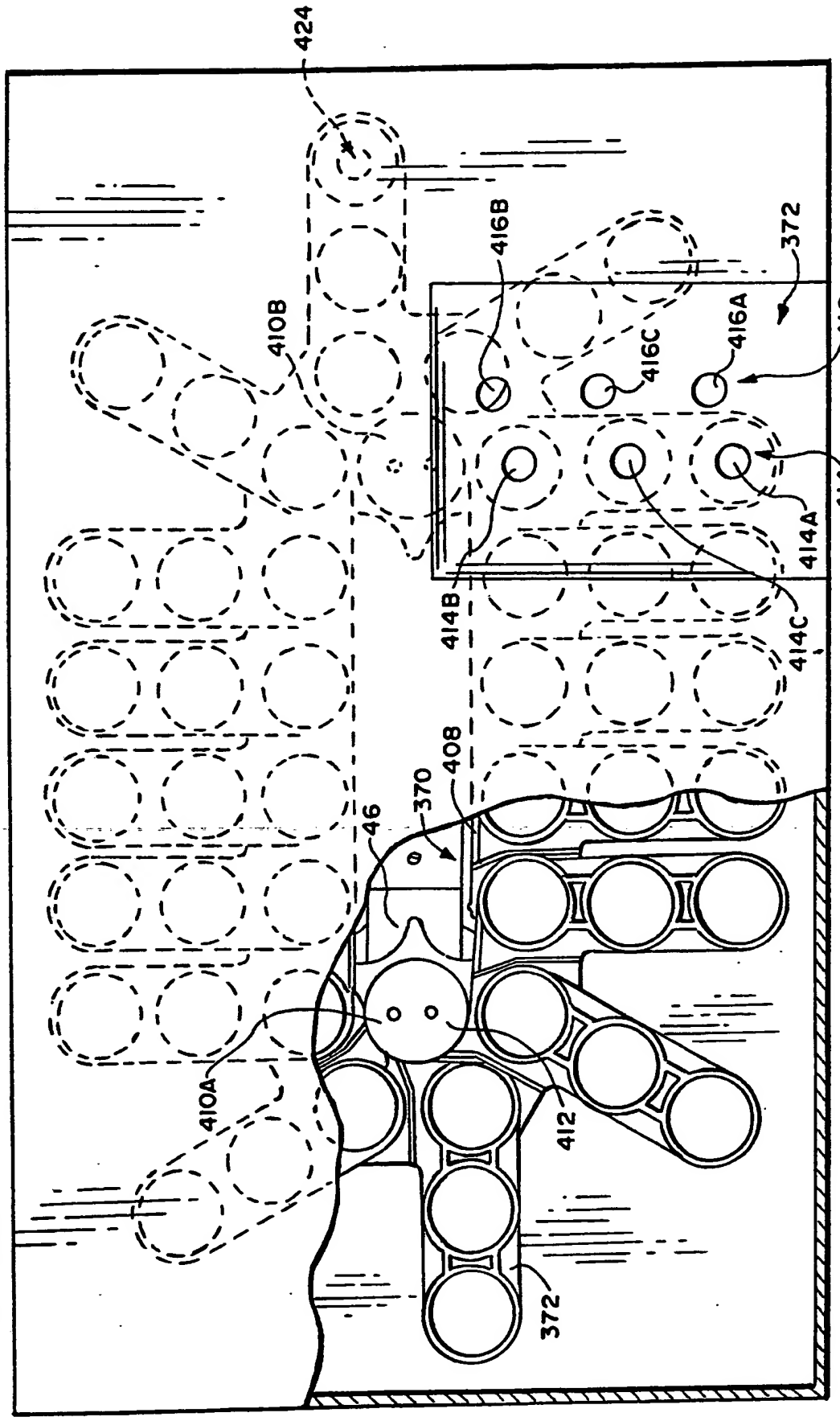

424
416B
372
410B
416A
416C
416
414
414A
414B
414C
408
370
46
410A
412
372

FIG. 49

FIG. 50

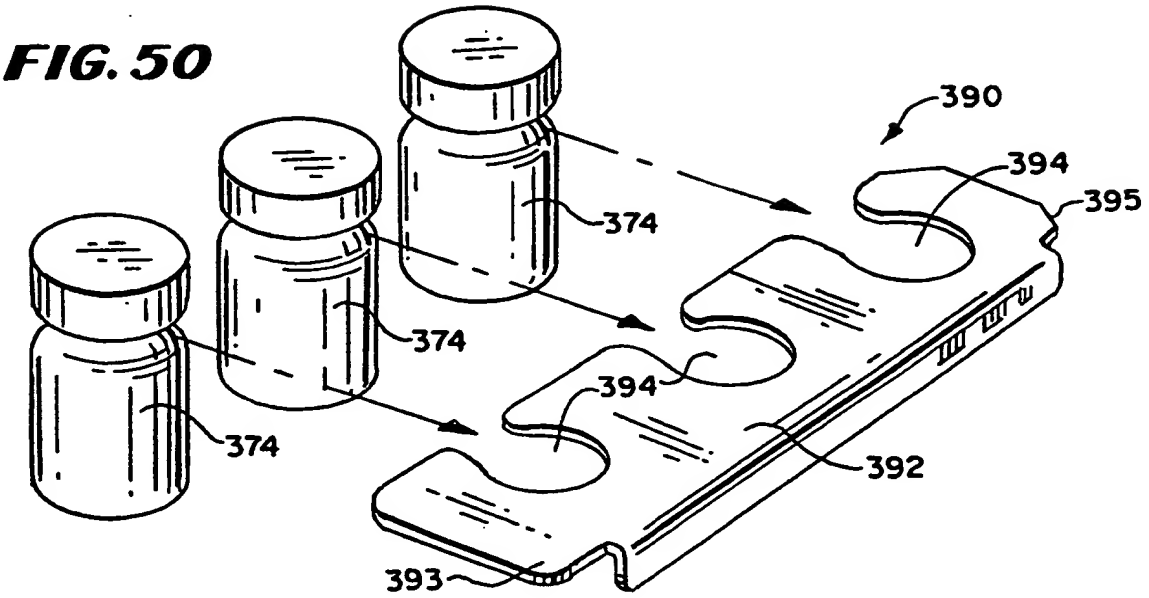
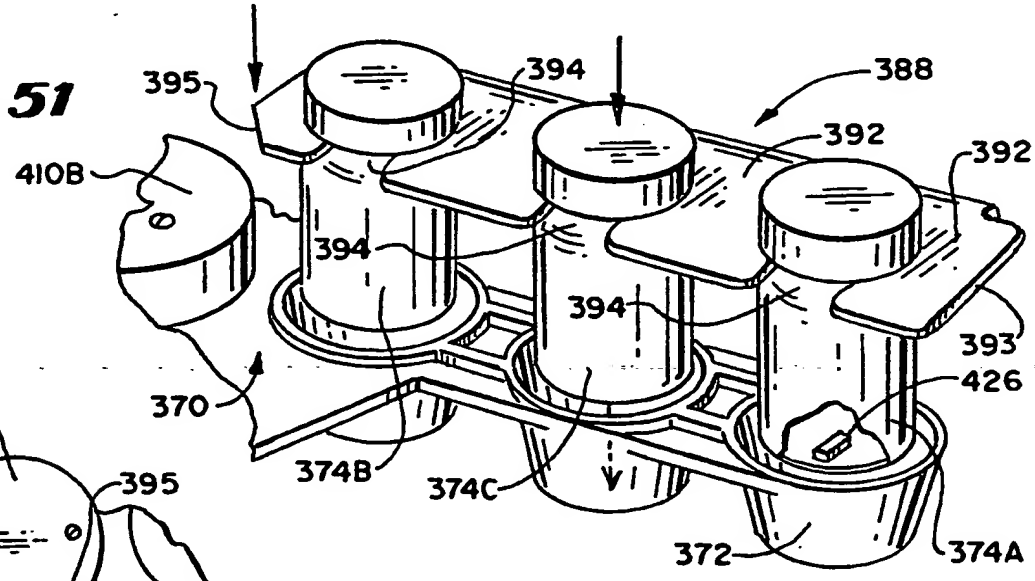


FIG. 51



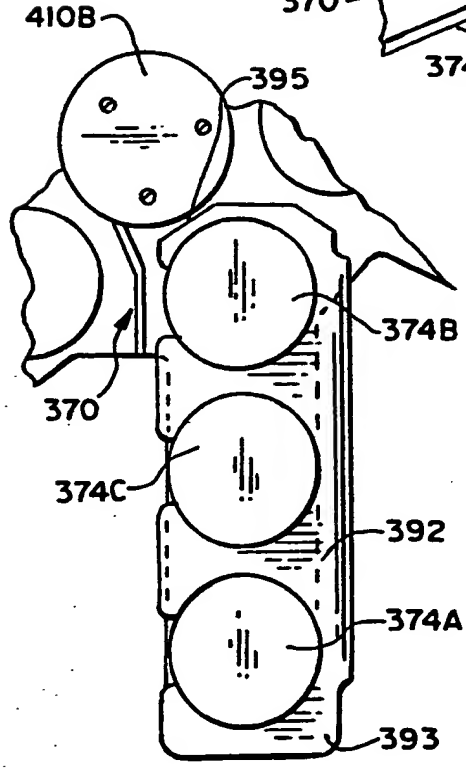
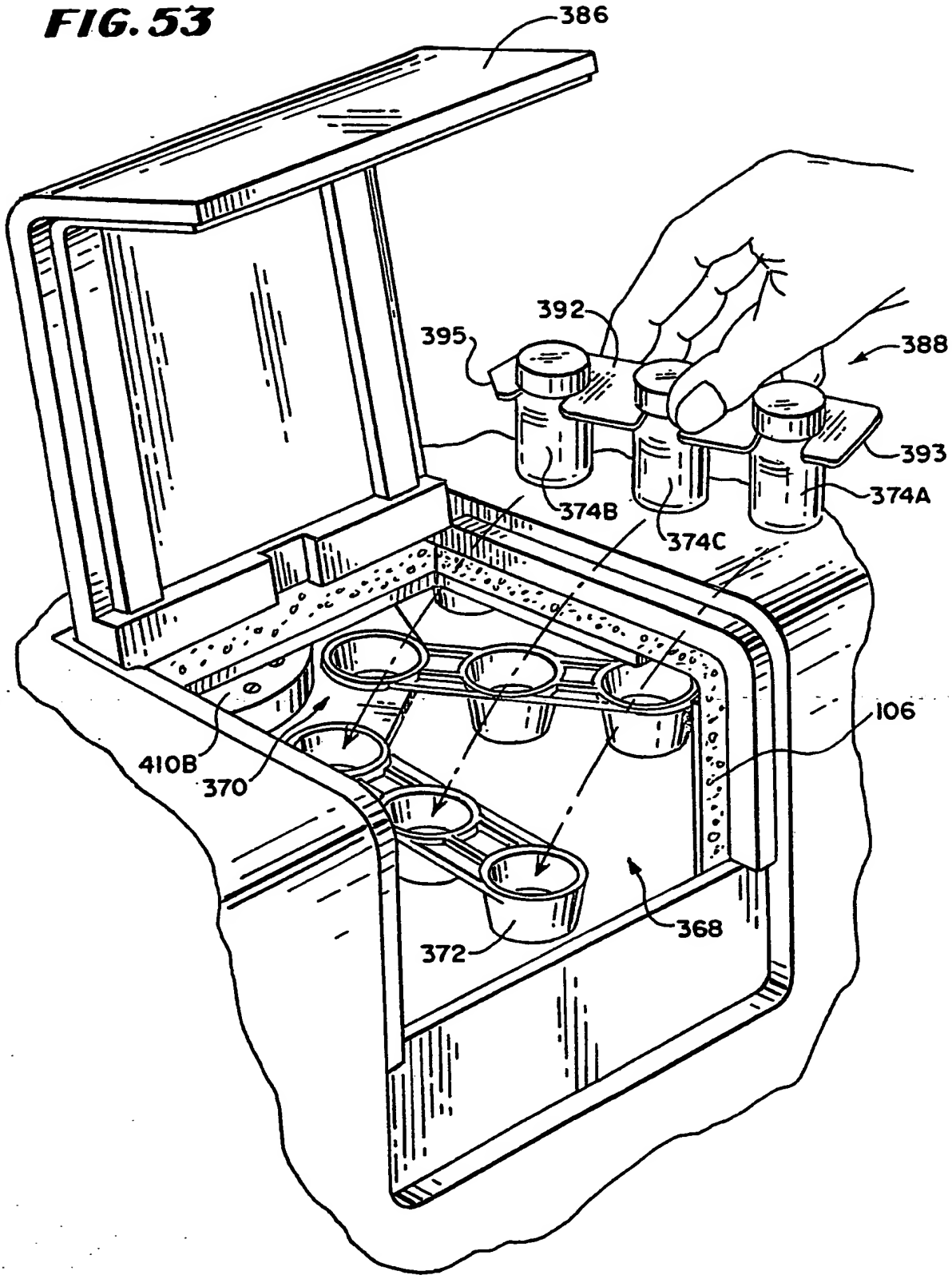


FIG. 52

FIG. 53



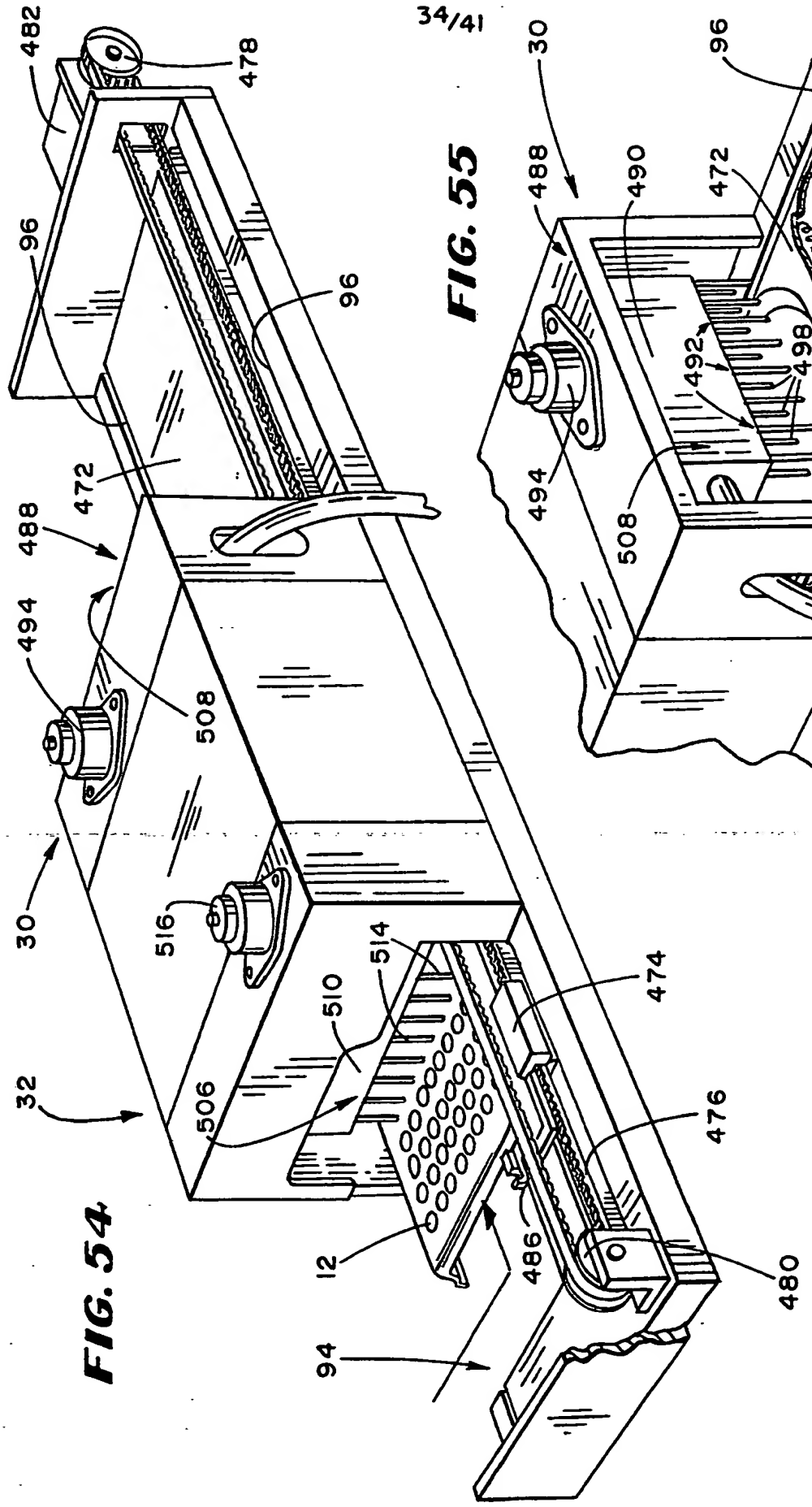

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FIG. 54

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FIG. 55

FIG. 56

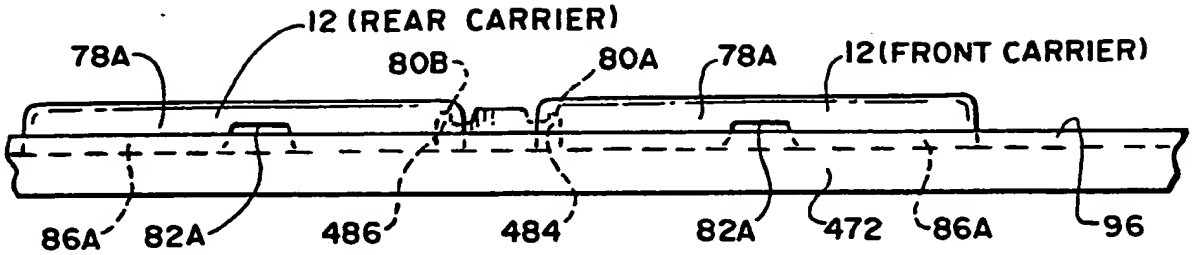


FIG. 57

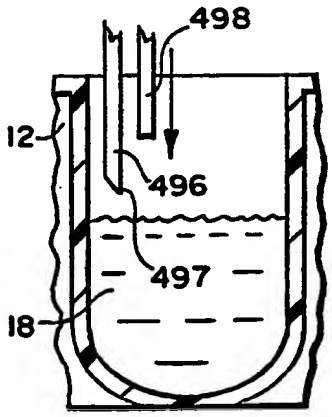


FIG. 58

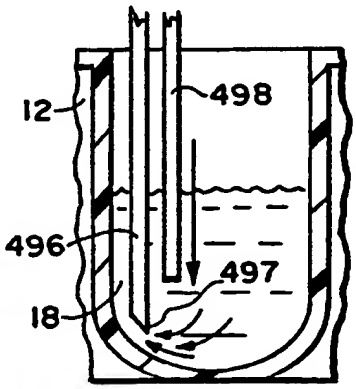


FIG. 59

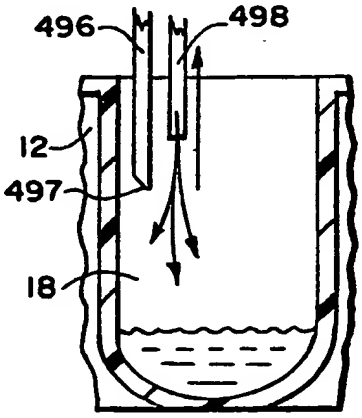
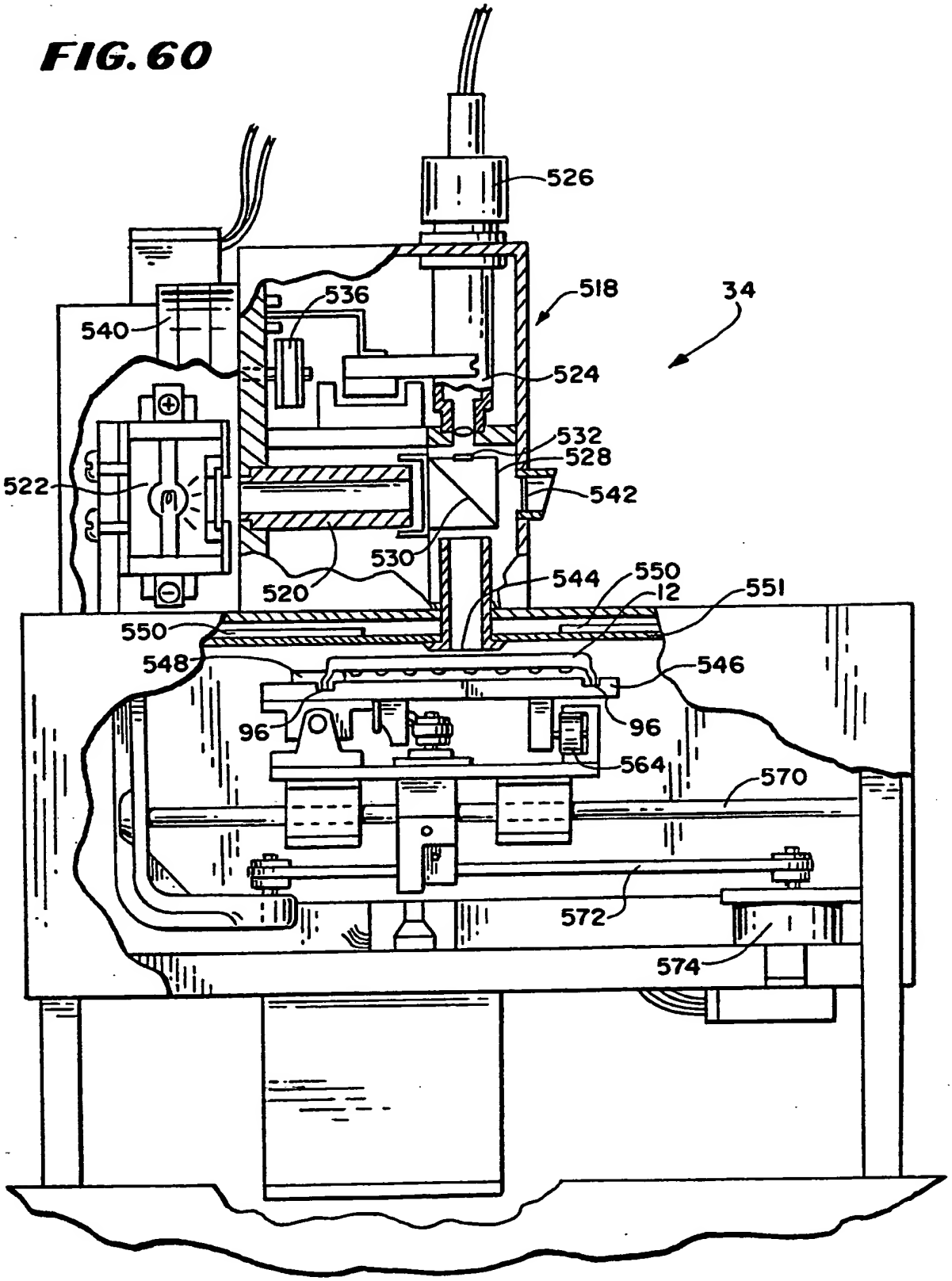


FIG. 60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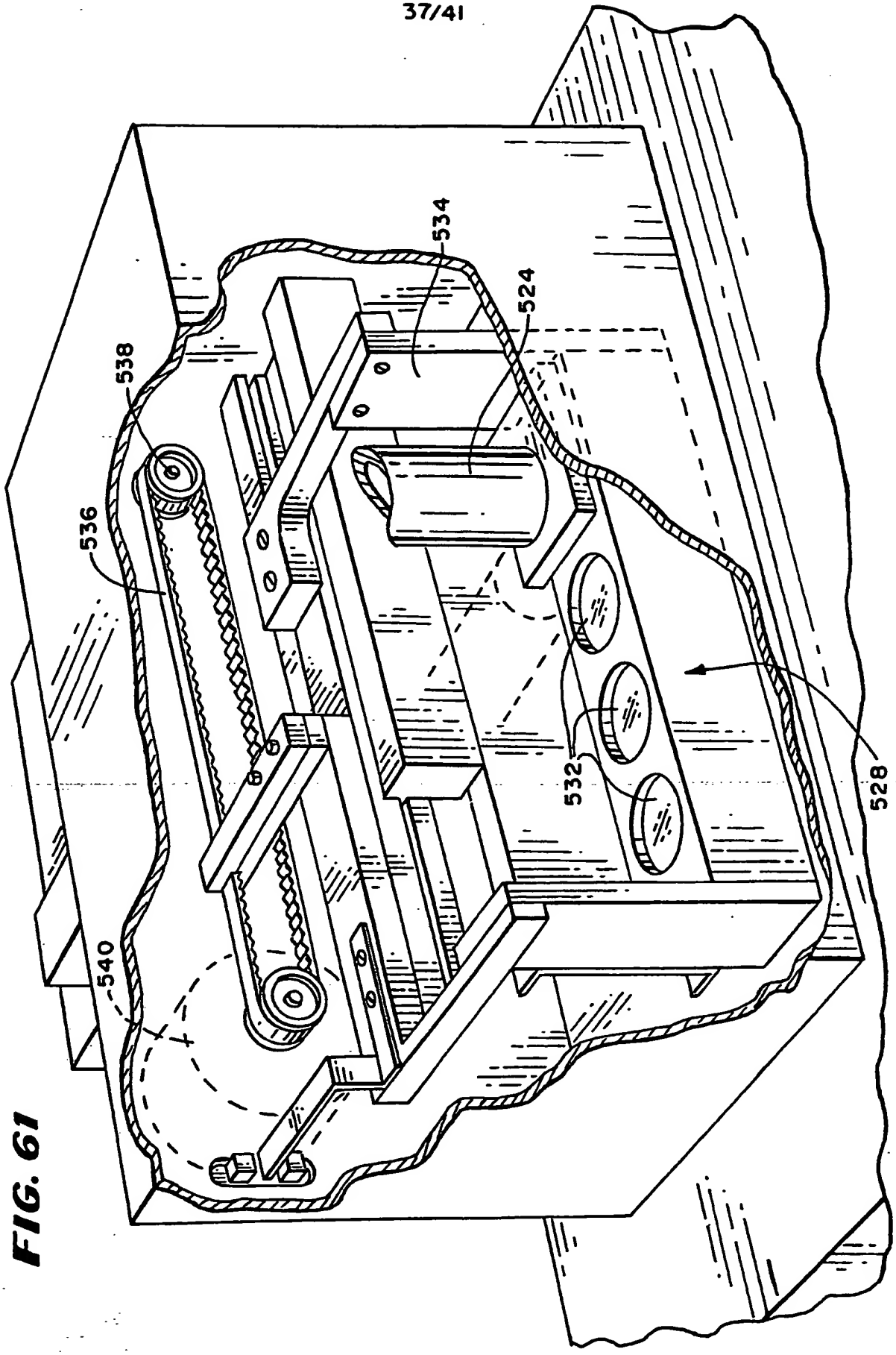

FIG. 61

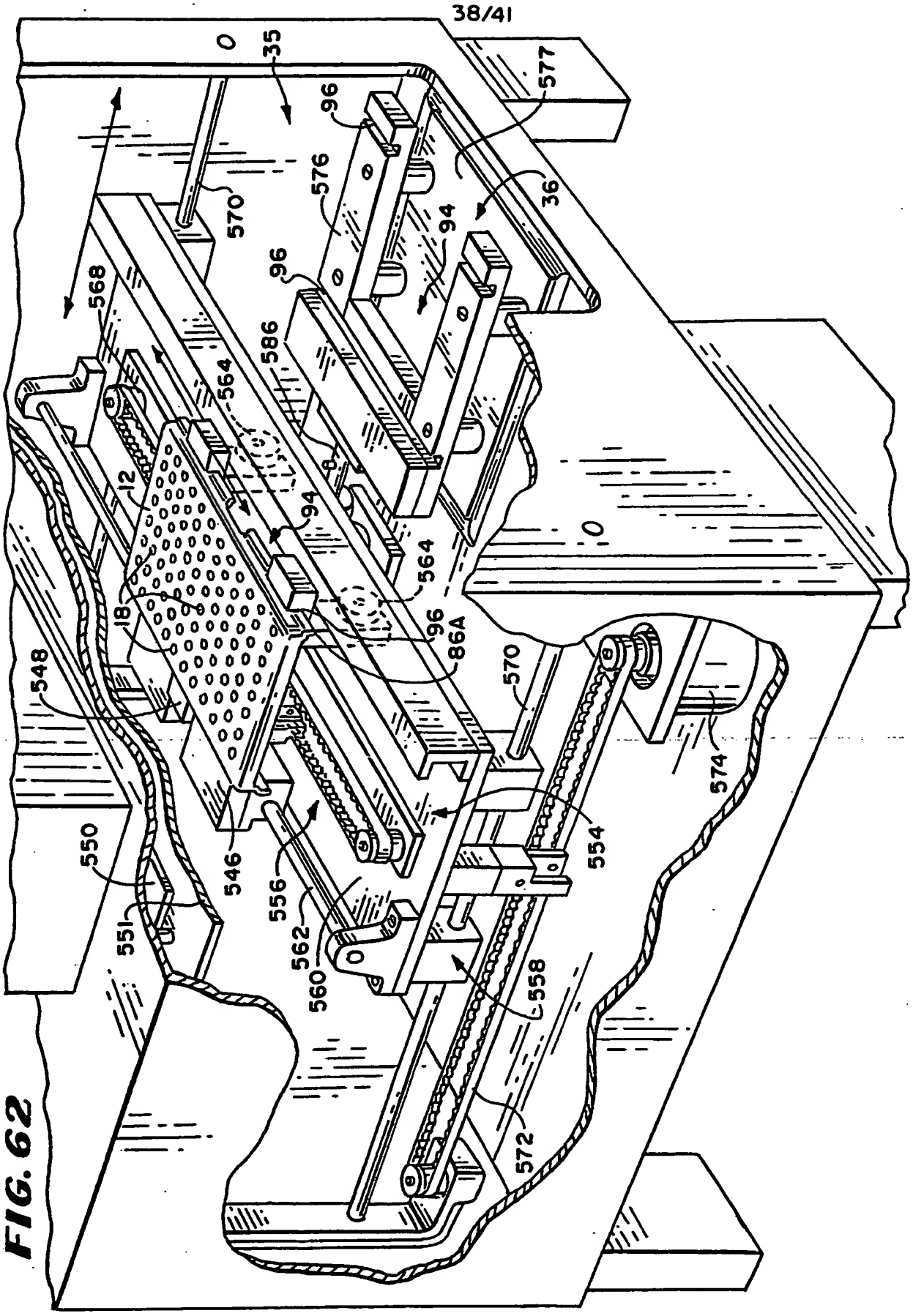
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FIG. 62

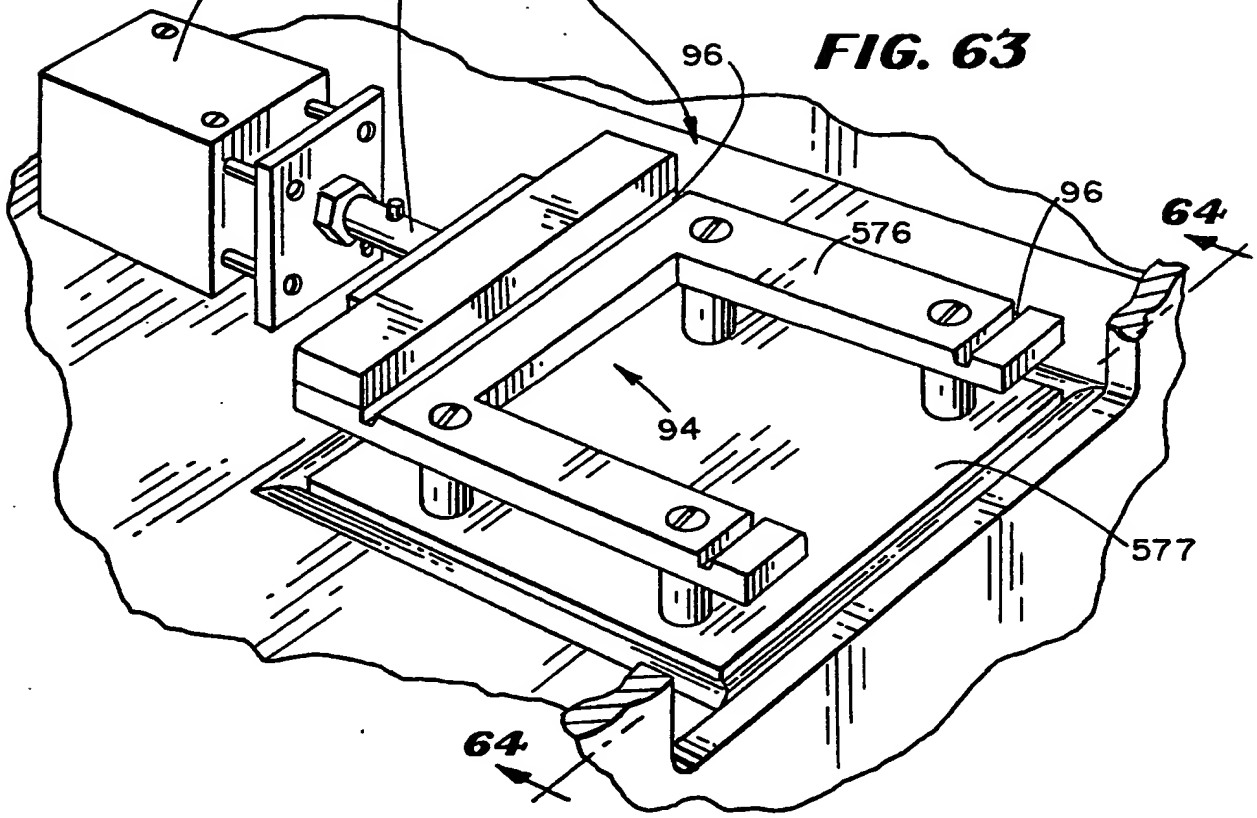
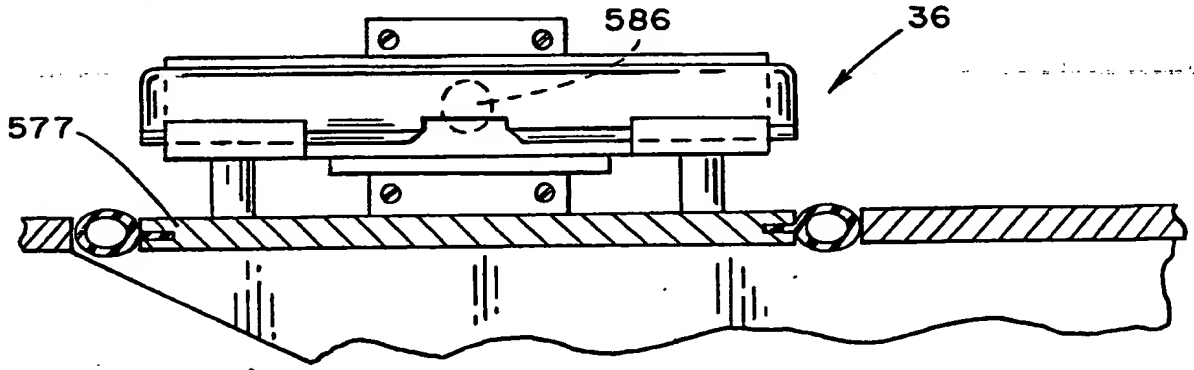


FIG. 63

FIG. 64



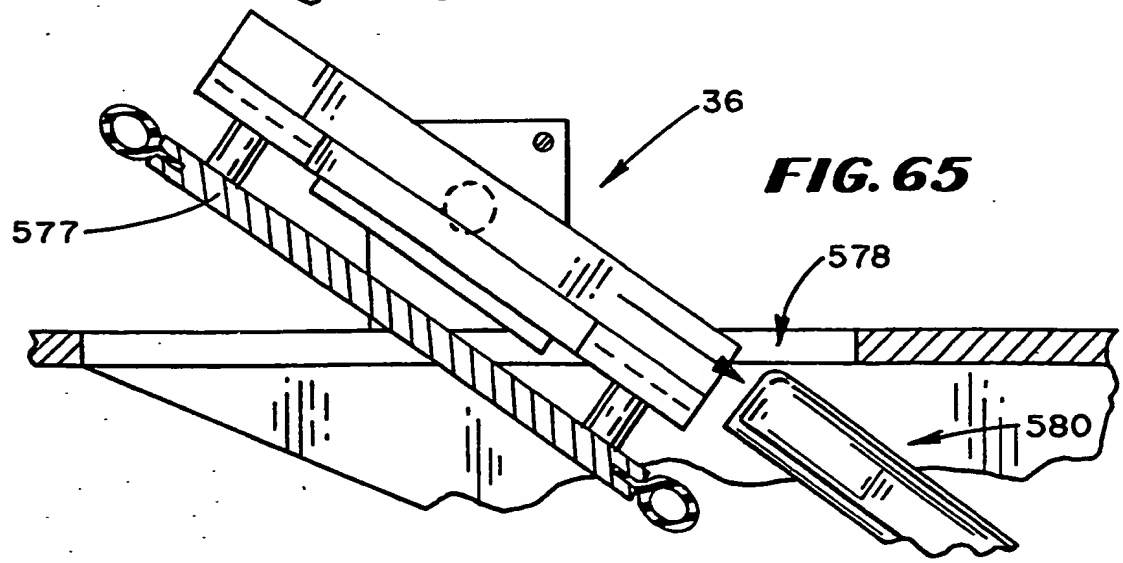


FIG. 65

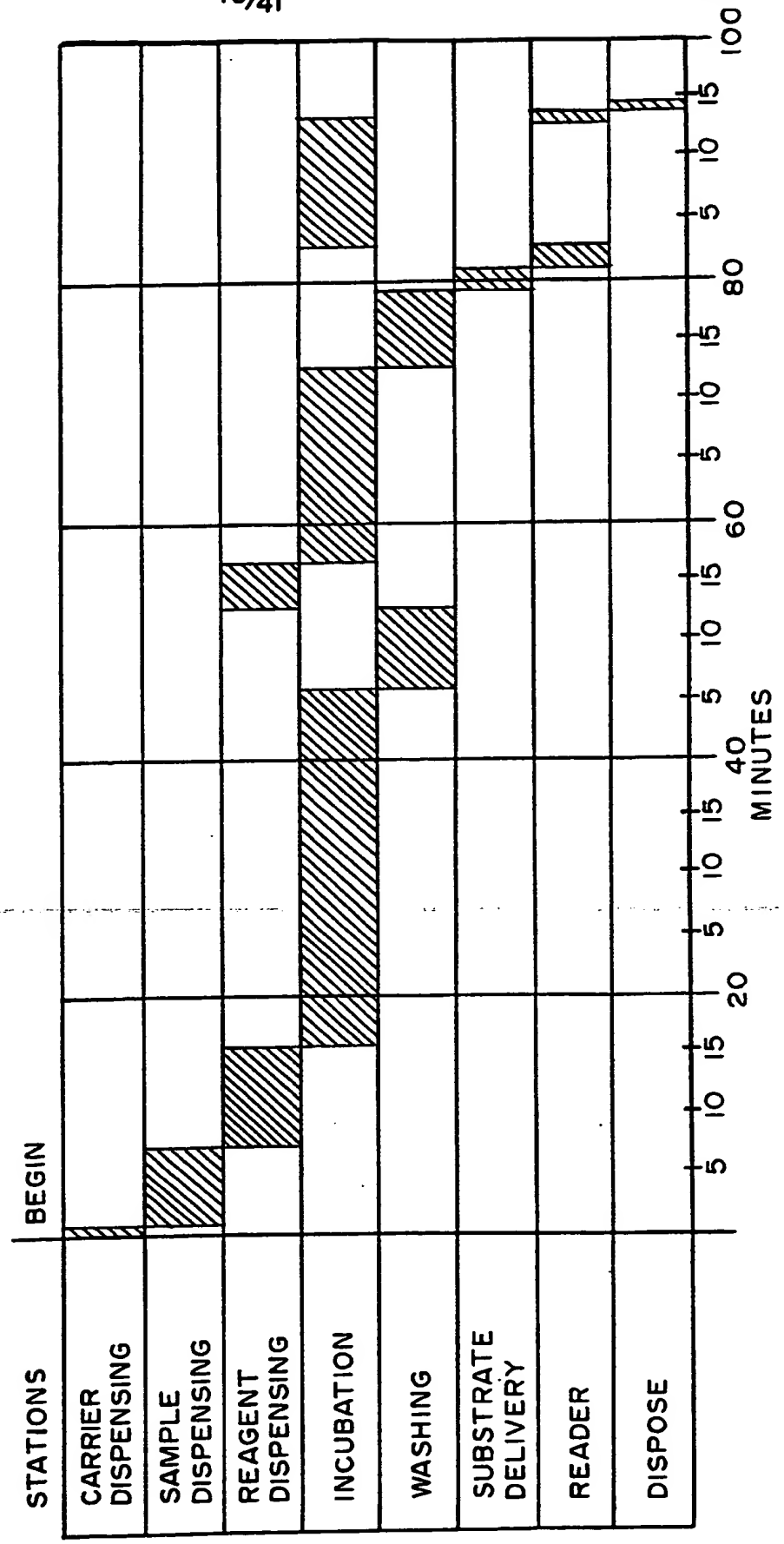
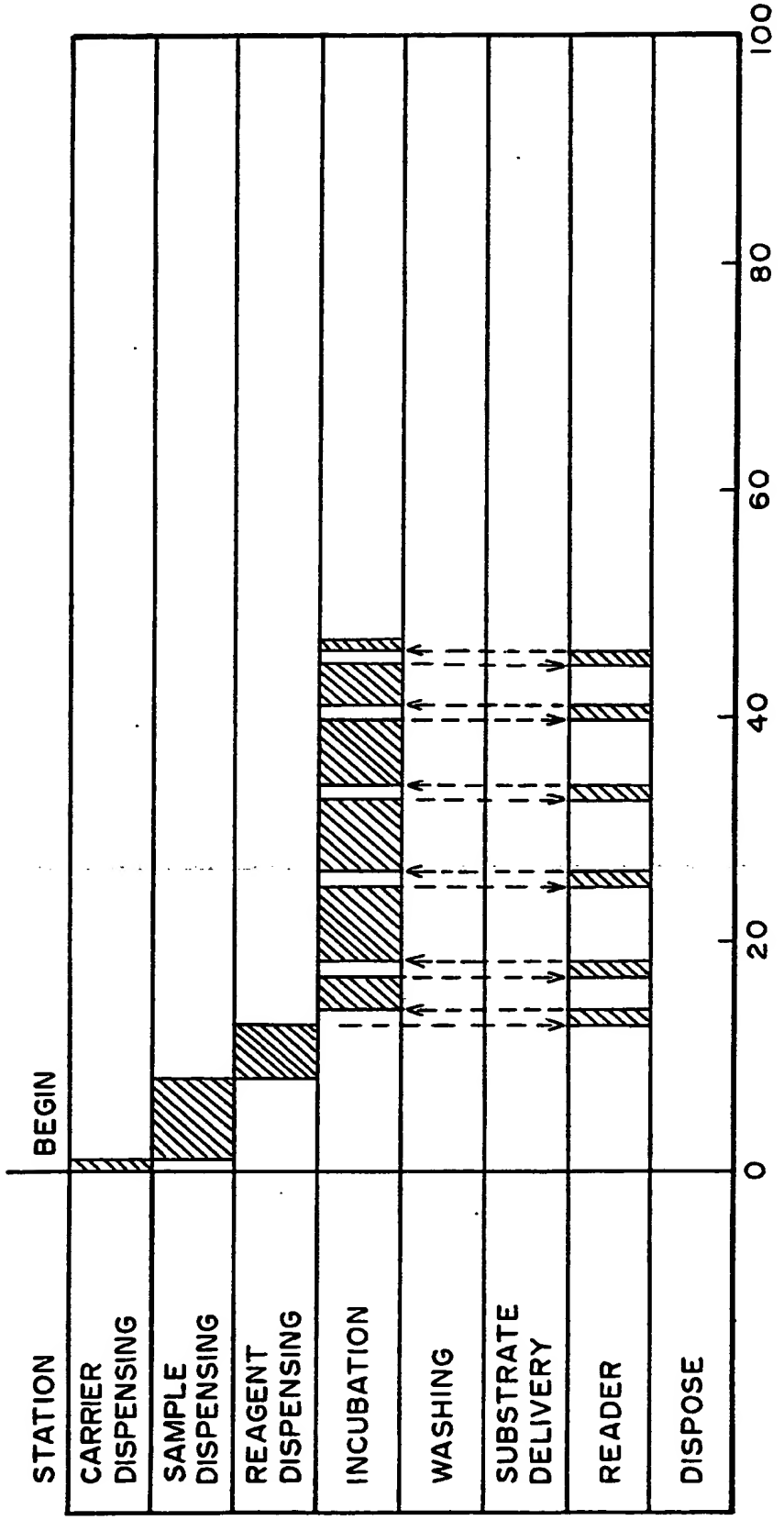

STATIONS
BEGIN
CARRIER DISPENSING
SAMPLE DISPENSING
REAGENT DISPENSING
INCUBATION
WASHING
SUBSTRATE DELIVERY
READER
DISPOSE
5 10 15 20 5 10 15 40 5 10 15 60 5 10 15 80 5 10 15 100
MINUTES

FIG. 66


STATION
CARRIER DISPENSING
SAMPLE DISPENSING
REAGENT DISPENSING
INCUBATION
WASHING
SUBSTRATE DELIVERY
READER
DISPOSE
BEGIN
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20
40
60
80
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FIG. 67

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/11133

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) :G01N 35/02
US CL :422/63, 65

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/63, 65, 64; 436/47, 48

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 3,193,359 (Baruch et al) 06 July 1965, entire document.	1-3, 9, 13, 16, 23-26
Y	US, A, 3,533,744 (Unger) 13 October 1970, entire document.	1-3, 10-14, 17-18, 23-26
Y	US, A, 3,912,456 (Young) 14 October 1975, claims 10-11.	16, 19-22
X	US, A, 4,113,436 (Werder et al) 12 September 1978, entire	1-2, 23
Y	document.	4, 8, 13, 24-26
Y	US, A, 4,265,855 (Mandle et al) 05 May 1981, entire document.	1-3, 13-14, 19-20, 23-26

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 February 1993	16 MAR 1993
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. NOT APPLICABLE	Authorized officer JAMES C. HOUSEL Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US92/11133

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,299,796 (Hogen Esch) 10 November 1981, entire document.	15
Y	US, A, 4,459,265 (Berglund) 10 July 1984, entire document.	1-3, 13, 23, 26
Y	US, A, 4,643,879 (Hanaway) 17 February 1987, entire document.	1, 3, 13, 23, 25-30
Y	US, A, 4,675,162 (Sakamaki et al) 23 June 1987, entire document.	4-7
Y	US, A, 4,966,853 (Matsuda et al) 30 October 1990, entire document.	1, 13, 23, 25
Y,P	US, A, 5,104,621 (Pfost et al) 14 April 1992, entire document.	10-12, 14-15, 18-20
Y,P	US, A, 5,122,342 (McCulloch et al) 16 June 1992, entire document.	7, 25-30